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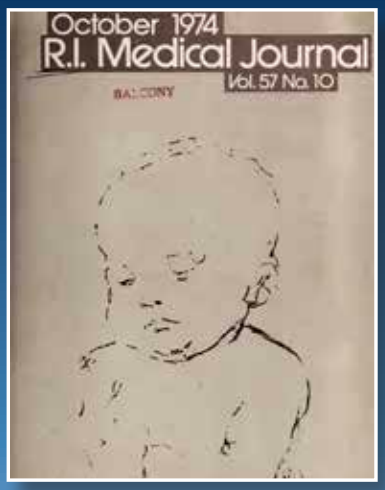

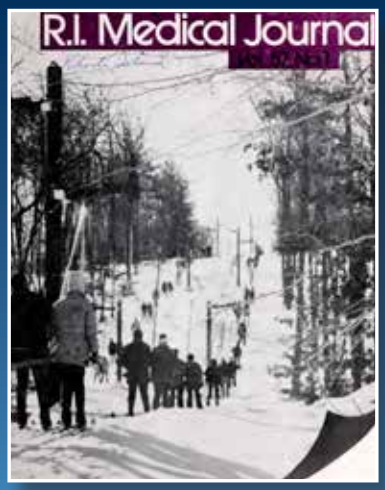

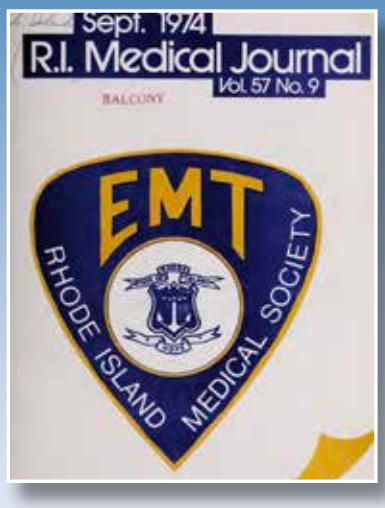

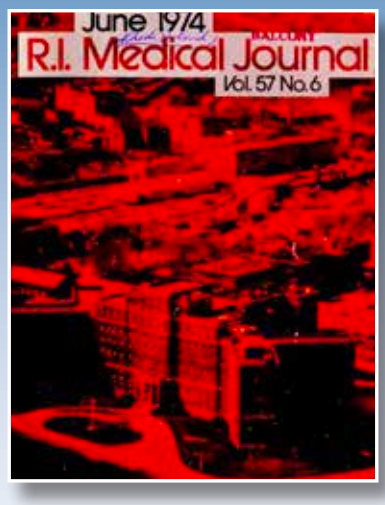

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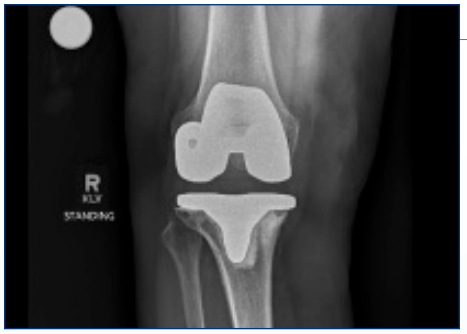

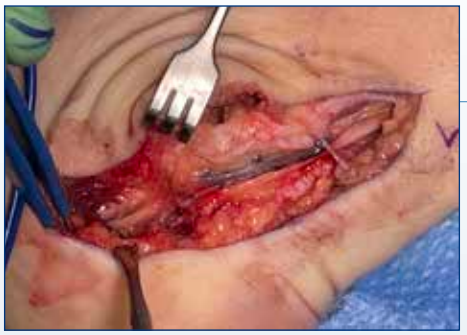

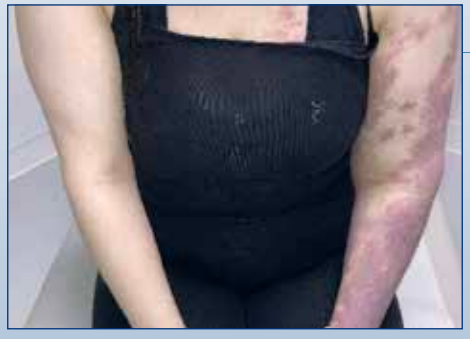

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Positive Culture of Atypical *Mycobacterium Avium* Following Revision Total Knee Arthroplasty

JONATHAN LIU, MD; JACOB LAPERCHE, BS, MD'24; MARGUERITE NEILL, MD; DEREK JENKINS, MD

ABSTRACT

CASE: We report a rare case of mycobacterial periprosthetic joint infection (PJI) after primary total knee arthroplasty 14 years earlier. Progressive knee pain over three years with a negative PJI infectious workup led to revision total knee arthroplasty. A surprising result was isolation of *Mycobacterium avium* from tissue cultures taken at time of revision surgery. After six months of antibiotic treatment, the patient is alive with well-functioning pain-free TKA at over one-year follow-up.

CONCLUSION: Periprosthetic joint infection can present acutely or chronically years following total knee arthroplasty. Depending on the infecting organism, patients can present with sepsis, or a more indolent slower course that mimics aseptic loosening. In the absence of positive pre-operative labs and cultures, and based on the Musculoskeletal Infection Society (MSIS) criteria, aseptic loosening is a diagnosis of exclusion. An atypical infectious organism should be considered a possible cause and may require specialized cultures of operative specimens.

KEYWORDS: *Mycobacterium avium*, revision total knee arthroplasty, prosthetic joint infection

INTRODUCTION

In the last 20 years, the number of total knee arthroplasties (TKA) performed worldwide has steadily increased, and with that there have been increasing numbers of periprosthetic joint infections (PJI).[1,2] PJI is among the most common reasons for revision TKA.[2,3] Common bacterial causes of PJI include staphylococcus aureus, staphylococcus epidermidis and enterococcus faecalis.[4] Mycobacteria as a cause of PJI is quite unusual, accounting for only 0.5%.[5]

Gold-standard treatment for patients with PJI is generally considered two-stage revision with removal of hardware, antibiotic spacer placement, and IV and oral antibiotic treatment, followed by a second surgery to reimplant knee hardware. Single-stage revision has been reported to have acceptable outcomes in some clinical scenarios.[3,6] The decision to revise a TKA is often preceded by advanced imaging to evaluate for evidence of osteolysis, labs including ESR and CRP, synovial fluid aspirate, microscopic analysis, and culture in accordance with MSIS criteria.[7] Patients with evidence of component loosening and clinical symptoms limiting their function can be indicated for revision arthroplasty aimed at attaining a well-fixed stable joint replacement. Even with a preoperative work-up of low suspicion for infection, patients may later be diagnosed with infection based on results of intra-operative cultures at the time of revision surgery.[8,9] Pragmatism dictates obtaining an odd number of cultures at revision so there is a tiebreaker sample if needed. If cultures return with unexpected growth after revision surgery, treatment algorithms have been suggested with retention of implants and targeted antibiotic therapy.[10] When an unexpected organism is isolated, the question arises whether the result is a true infection or a contaminant.

We report a patient with non-insulin dependent diabetes mellitus (NIDDM) who was 14 years status post-primary TKA and presented with over one year of knee pain. After low-suspicion infectious work-up, with a mildly elevated CRP 11.8 mg/ml (reference <5 mg/ml) and otherwise normal laboratory and synovial aspirate values, the TKA was revised. However, a non-tuberculous mycobacterium (NTM) was isolated from two of three intra-operative smears and subsequent tissue culture. The patient was treated with a three-drug regimen for six months and is pain free at 1.5 years follow-up.

Consent: Verbal consent was obtained from the patient for this case report.

CASE REPORT

A 78-year-old woman with NIDDM had an uncomplicated right TKA in 2008. In 2022, she presented with slowly progressive knee pain affecting her mobility. On exam, the right knee range of motion was 0 to 120 degrees, stable to varus and valgus stress throughout flexion extension arc. Plain radiographs showed lucency suggesting polyethylene wear and osteolysis (**Figure 1).** CT scan confirmed lucencies anterior to tibial keel and medial aspect of tibial tray (**Figure 2A, 2B)** and about the femoral component**.** Pre-operative knee aspirate yielded 975 nucleated cells, 1% polymorphonuclear leukocytes, and no aerobic or anaerobic growth of aspirate cultures at 14 days. She failed a trial of conservative therapy over several months and was scheduled for revision TKA for presumed aseptic loosening due to polyethylene bearing

Figure 1. Anteroposterior X-ray of patients' right knee at the time of presentation.

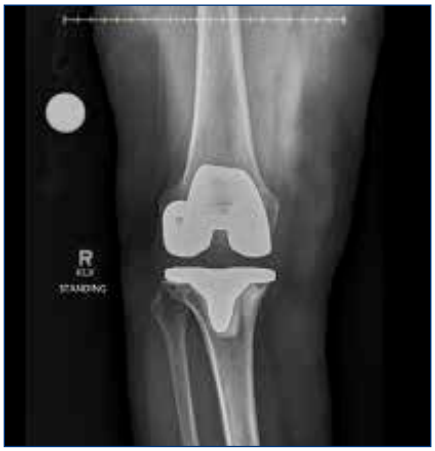


Figure 2A. Coronal CT images of patients' right knee taken pre-operatively.

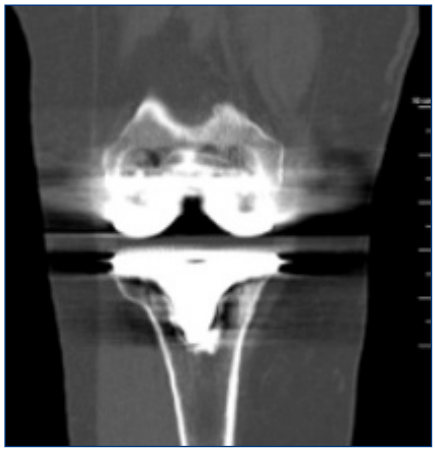
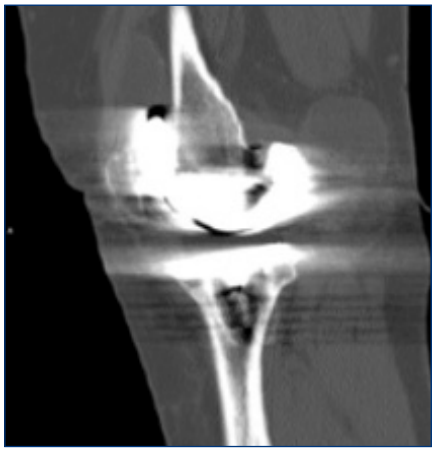


Figure 2B. Sagittal CT images of patients' right knee taken pre-operatively.



wear and osteolysis. Intra-operatively, a standard midline incision was made through patient's previous scar. The patella component was found to be well-fixed. Three specimens were sent for bacterial, fungal and AFB cultures. Bacterial and fungal cultures were negative at 14 days. Two of three specimens had a positive AFB smear and AFB culture was positive at day 13 in culture. The isolate was identified as *Mycobacterium avium intracellulare* (MAI) by mass spectrometry. The result was surprising given the patient's lack of immunosuppression. Lab contamination was ruled out by whole genome sequencing of the two isolates from two other culture-positive mycobacterial specimens obtained from different patients processed the same day. These isolates were determined to be non-MAI mycobacterial species.

The patient denied fevers, chills or night sweats, and had not been on systemic steroids or immunomodulator medications. The patient was treated with ethambutol, azithromycin and rifampin daily for six months with monitoring of labs, EKG, and visual acuity and color discrimination. Post-operative imaging showed well-aligned and fixed implants which remained true at two weeks and one year post-operatively **(Figures 3, 4A, 4B)**. The patient was without pain or signs of infection at one year with excellent knee stability and knee range of motion 0–120 degrees.

Figure 3. Two-week post-operative X-ray of patients' right knee.

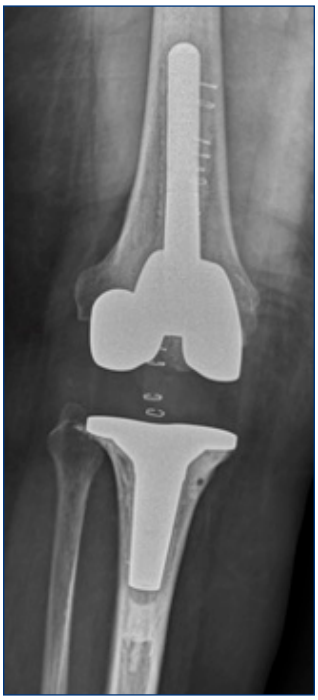


Figure 4A. One-year post-operative anteroposterior X-ray of patients' right knee.

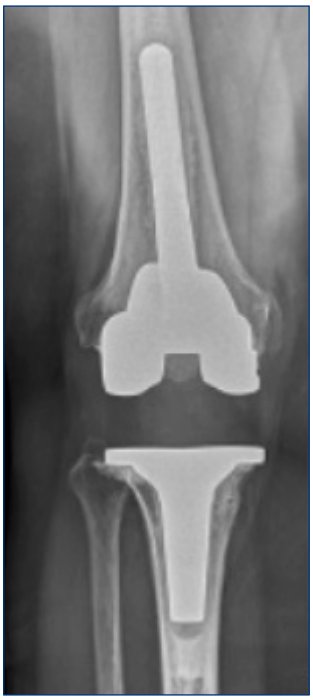
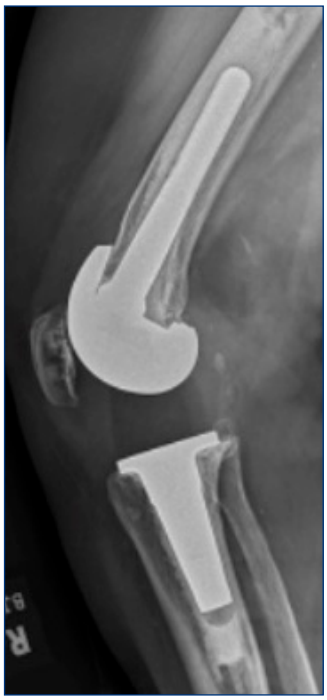


Figure 4B. One-year post-operative lateral X-ray of patients' right knee.



DISCUSSION

This case reports a rare occurrence of *M. avium* positive intra-operative culture during revision TKA for chronic knee pain 14 years after primary TKA in an otherwise healthy patient with well-controlled DM. Non-tuberculous mycobacteria (NTM) infections of prosthetic joints have been reported previously but are rare. Ingraham et al report a case of a 74-year-old with *Mycobacterium avium-intracellulare* PJI of the hip 15 years after primary total hip arthroplasty with previous revisions five and 10

years ago. This patient had multiple comorbidities including rheumatoid arthritis (RA) on prednisone, leflunomide and infliximab, Alzheimer's dementia, and coronary artery disease. Due to comorbidities the patient was treated with antibiotics, and incision and drainage of the hip. Four months of therapy did not resolve the infection and the patient expired six months after presentation.[11] Maimaiti et al reported six cases of NTM PJI following total joint arthroplasty with a mean onset of four months post-surgery. There was only one case of *M. avium*, which was the slowest growing of the NTM infections.[12]

Risk factors that have been identified for NTM infection include increasing age, BMI, lung disease, immunosuppressive therapies, and immunocompromised state.[13] The possibility of a false-positive culture from lab contamination was considered in our patient. This was ruled out by whole genome sequencing of the patient's isolate and two other mycobacterial isolates processed the same day which demonstrated different mycobacterial strains. The false-positive rate of *Mycobacterium avium-intracellulare* in prosthetic joint cultures has not been reported; however, the false positive rate of *Mycobacterium tuberculosis* (TB) has been reported to be around 2% secondary to lab cross-contamination and around 15% with a single-positive as well as a negative culture.[14] The decision to treat, despite the presence of significant risk factors for this infection, was ultimately based on the risk of significant morbidity if this was a true infection that, in the absence of treatment, would become a more advanced infection in the future.

The incidence of extrapulmonary *M. tuberculosis* has been more widely reported in the literature. Of the total extrapulmonary cases in the US from 2010 to 2019, approximately 9–11% of a total 1,800 to 2,400 cases per year involve bones or joints.[15] Though rare, there have been a few case reports of TB PJI reporting various outcomes and risk factors that may have been associated with this rare occurrence.[16,17] Risk factors for TB PJI, and likely *Mycobacterium avium-intracellulare* PJI, include immunocompromised state, travel to endemic regions, and prior or latent infections. Treatment options are typically antibiotic therapy combined with surgical management, including debridement, wash-outs, and revisions in cases of PJI.[17]

This case highlights the rarity and challenges associated with diagnosis and treatment of an *M. avium* PJI. Our patient was not immunosuppressed, and had well-controlled diabetes, which initially decreased our pre-diagnostic suspicion of atypical mycobacterium infection. The AFB smears of two specimens were positive, making accidental contamination unlikely. To enhance the likelihood of culture growth, the three specimens were pooled for culture, and it was positive after 13 days. The necessity of advanced testing and longer culture incubation time presented an initial barrier to rapidly starting treatment. In the present case, with 2/3 positive AFB smear and a positive culture for *M. avium*, and once contamination was ruled out, discussions were held with the patient, the orthopaedic and infectious disease care team members, and the final decision was made to treat as an atypical PJI.

CONCLUSION

This case reports an unsuspected positive culture for *M. avium* from the knee following revision TKA for presumed aseptic loosening of knee implants despite the patient's lack of risk factors, and negative preoperative PJI screening per MSIS criteria. While this case presents an uncommon finding, the authors recommend a multidisciplinary discussion including the patient and infectious disease specialists to determine if positive cultures should be treated. In the absence of definitive clinical guidelines in such cases, the authors recommend multidisciplinary team discussions with expert consultants, use of best clinical judgment and appropriate antibiotic treatment to prevent untoward consequences of infection, further revisions, and other complications for the patient, while balancing the potential side effects and cost of treatment.

References

1. Delanois RE, Mistry JB, Gwam CU, Mohamed NS, Choksi US, Mont MA. Current Epidemiology of Revision Total Knee Arthroplasty in the United States. J Arthroplasty. 2017 Sep;32(9):2663-2668. PMID: 28456561.
2. Duncan ST, Schwarzkopf R, Seyler TM, Landy DC. The Practice Patterns of American Association of Hip and Knee Surgeons for the Management of Chronic Periprosthetic Joint Infection After Total Knee Arthroplasty. J Arthroplasty. 2023 Nov;38(11):2441-2446. PMID: 37142069.
3. Liukkonen R, Honkanen M, Skyttä E, Eskelinen A, Karppelin M, Reito A. Trends in Revision Knee Arthroplasty for Prosthetic Joint Infection: A Single-Center Study of 384 Knees at a High-Volume Center Between 2008 and 2021. J Arthroplasty. 2023 Nov;38(11):2447-2454. PMID: 37236284.
4. Migliorini F, Eschweiler J, Tingart M, Rath B. Posterior-stabilized versus cruciate-retained implants for total knee arthroplasty: a meta-analysis of clinical trials. Eur J Orthop Surg Traumatol. 2019 May;29(4):937-946. PMID: 30649620.
5. Patel R. Periprosthetic Joint Infection. N Engl J Med. 2023 Jan 19;388(3):251-262. PMID: 36652356.
6. Shichman I, Ward SA, Lu L, Garceau S, Piuzzi NS, Seyler TM, Schwarzkopf R. Failed 2-Stage Revision Knee Arthroplasty for Periprosthetic Joint Infection-Patient Characteristics and Outcomes. J Arthroplasty. 2023 Oct;38(10):2177-2182. PMID: 37179023.
7. Parvizi J, Tan TL, Goswami K, Higuera C, Della Valle C, Chen AF, Shohat N. The 2018 Definition of Periprosthetic Hip and Knee Infection: An Evidence-Based and Validated Criteria. J Arthroplasty. 2018 May;33(5):1309-1314.e2. PMID: 29551303.
8. Eriksson H, Lazarinis S. Low accuracy in preoperative tissue biopsies for diagnosing chronic periprosthetic joint infection: an observational retrospective single-centre study. J Int Med Res. 2023 Jun;51(6):3000605231158972. PMID: 37389568.
9. Schwarze J, Moellenbeck B, Gosheger G, Puetzler J, Deventer N, Kalisch T, Schneider KN, Klingebiel S, Theil C. The Role of Single Positive Cultures in Presumed Aseptic Total Hip and Knee Revision Surgery-A Systematic Review of the Literature. Diagnostics (Basel). 2023 May 8;13(9):1655. PMID: 37175046.

10. Leone JM, Hanssen AD. Management of infection at the site of a total knee arthroplasty. J Bone Joint Surg Am. 2005 Oct;87(10):2335-48. PMID: 16224857.
11. Ingraham NE, Schneider B, Alpern JD. Prosthetic Joint Infection due to *Mycobacterium avium-intracellulare* in a Patient with Rheumatoid Arthritis: A Case Report and Review of the Literature. Case Rep Infect Dis. 2017;2017:8682354. PMID: 28280641.
12. Maimaiti Z, Li Z, Xu C, Fu J, Hao L, Chen J, Li X, Chai W. Non-Tuberculosis Mycobacterium Periprosthetic Joint Infections Following Total Hip and Knee Arthroplasty: Case Series and Review of the Literature. Orthop Surg. 2023 Jun;15(6):1488-1497. PMID: 37154097.
13. Liu Q, Du J, An H, Li X, Guo D, Li J, Gong W, Liang J. Clinical characteristics of patients with non-tuberculous mycobacterial pulmonary disease: a seven-year follow-up study conducted in a certain tertiary hospital in Beijing. Front Cell Infect Microbiol. 2023 Jun 22;13:1205225. PMID: 37424783.
14. Barac A, Karimzadeh-Esfahani H, Pourostadi M, Rahimi MT, Ahmadpour E, Rashedi J, Mahdavipoor B, Kafil HS, Spotin A, Abate KH, Mathioudakis AG, Asgharzadeh M. Laboratory Cross-Contamination of Mycobacterium tuberculosis: A Systematic Review and Meta-analysis. Lung. 2019 Oct;197(5):651-661. PMID: 31203380.
15. Table 15 | Reported TB in the US 2019 | Data & Statistics | TB | CDC. https://www.cdc.gov/tb/statistics/reports/2019/table15.htm (2023).
16. Elzein FE, Haris M, Alolayan SS, Al Sherbini N. Total knee prosthesis infected with *Mycobacterium tuberculosis*. BMJ Case Rep. 2017 Sep 7;2017:bcr2017220596. PMID: 28883009.
17. Lo CKL, Chen L, Varma S, Wood GCA, Grant J, Wilson EW. Management of *Mycobacterium tuberculosis* Prosthetic Joint Infection: 2 Cases and Literature Review. Open Forum Infect Dis. 2021 Aug 31;8(10):ofab451. PMID: 34631919.

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Refractory Hypoglycemia Due to Sulfonylurea Contamination of Illicit Opioid Medications

JEFFREY R. SAVARINO, MD, MPH; ROBERT MOKSZYCKI, PharmD; ROBERT TUBBS, MD; RACHEL S. WIGHTMAN, MD

ABSTRACT

Illicit drug supply adulteration can heighten the risk for adverse health outcomes. Sulfonylurea medications are widely used in the treatment of diabetes mellitus (DM). Unintentional or intentional overdose of sulfonylureas can cause refractory hypoglycemia. This case report describes a 62-year-old male patient who presented to the emergency department (ED) after being found on the ground with signs of mild trauma. He was noted to be persistently hypoglycemic despite boluses of intravenous dextrose, a dextrose infusion, and oral nutrition. The patient did report purchase and oral ingestion of pills sold as oxycodone and that the pill shape and color were different from his usual supply. The patient was empirically treated with octreotide resulting in normalization of his serum glucose. Testing demonstrated a serum glipizide concentration six times the reporting range. This case represents unintentional sulfonylurea exposure in the setting of non-prescribed oxycodone use, resulting in hypoglycemia refractory to intravenous dextrose and oral nutrition. Octreotide is an additional potential treatment for this condition. As in this case, ingestion of street drugs may present a potential source of sulfonylurea exposure. Opioid contamination with sulfonylureas has not been widely reported in the literature and knowledge about this potential exposure is important for the prompt recognition and treatment of these patients by emergency physicians.

KEYWORDS: sulfonylureas, substance-related disorders, hypoglycemia

BACKGROUND

Sulfonylurea medications were first developed in the 1950s as oral medications to treat diabetes mellitus (DM).[1] Second-generation sulfonylureas are widely used in the management of DM, as they are inexpensive and effective.[1] Sulfonylureas bind to and inhibit potassium channels on beta cells located in the pancreas; the subsequent resting potential shift leads to calcium influx into beta cells, which then releases insulin into the bloodstream.[1,2] For patients with DM, the increased insulin secretion works to decrease blood glucose concentrations and improve hyperglycemia.[1,2] Sulfonylurea-mediated insulin release occurs regardless of a patient's initial blood glucose levels and patients with normal blood glucose levels who are exposed to sulfonylurea medication may experience persistent hypoglycemia.[1,3-5] Here we present a unique case report of a patient presenting with refractory hypoglycemia after exposure to counterfeit oxycodone pills contaminated or substituted with glipizide, a sulfonylurea.

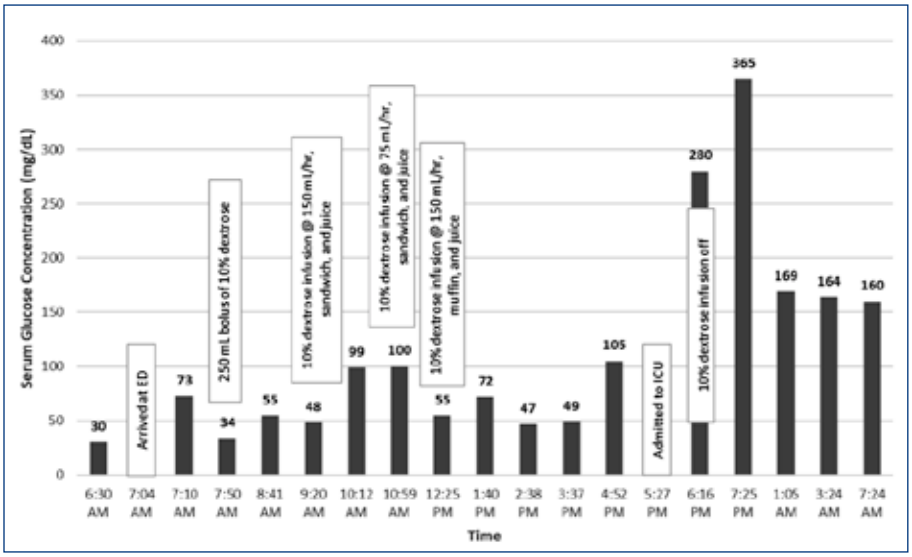
CASE REPORT

A 62-year-old male patient with a history of chronic back pain presented to the emergency department (ED) after being found on the ground outside his apartment. Emergency medical personnel noted abrasions to his face and extremities. The patient was initially lethargic and confused but was opening his eyes spontaneously and following commands. The patient's blood prehospital glucose was 30 mg/dL, and the patient was given 12.5 gm of dextrose 10% (D10). His mental status improved, and he was no longer confused upon arrival at the ED, although he was still amnestic to the preceding events. Trauma workup, including Computed Tomography (CT) of the brain, cervical spine, chest, abdomen, pelvis, and back, was negative for acute injury. The patient's history and medications were reviewed. He denied a history of diabetes, use of insulin, or known ingestion of any glucose-lowering medications.

The patient's glucose upon arrival at the ED was 73 mg/dL **(Figure 1)**. This was checked one hour later and was 34 mg/dL. An additional 25 gm bolus of D10 was administered with only a minimal increase in his blood glucose to 55 mg/dL. He was then started on a D10 infusion at 150 mL/hr. Once his trauma evaluation was complete, he was fed multiple calorie-rich meals. The patient's glucose rose to 100 mg/dL several hours after the D10 infusion was initiated, but the glucose rapidly dropped to 55 mg/dL after the rate of the D10 infusion was lowered to 75 mL/hr.

Medical history was expanded due to persistent, undifferentiated hypoglycemia. No infectious signs or symptoms were reported. While the patient did consume alcohol frequently, he did not have laboratory evidence of hepatic dysfunction and a review of his dietary habits did not yield any concern for glycogen deficiency. Upon directed questioning,

Figure 1. Serum glucose monitoring and medications administered during the hospital course in a patient with counterfeit oxycodone exposure with contamination with glipizide.



*EMS = Emergency Medical Services; ED = Emergency Department; ICU = Intensive Care Unit

the patient finally admitted to illicit purchase of presumed oxycodone from a street vendor to treat chronic low back pain. He noted that the pill shape was different than his usual supply. The patient consumed several of these pills the night prior to his ED presentation. A urine drug screen tested positive only for oxycodone. A serum sulfonylurea detection assay was ordered, and the patient was empirically treated with octreotide 100 mg subcutaneously with resolution of his hypoglycemia shortly thereafter. The patient was admitted to the intensive care unit with eventual discontinuation of his D10 infusion after a total of 12 hours. His testing returned with a serum glipizide concentration of 240 ng/mL.

DISCUSSION

This case represents an inadvertent ingestion of glipizide, a type of sulfonylurea, resulting in hypoglycemia refractory to intravenous dextrose and oral nutrition. Contamination of prescription or illicit pharmaceuticals sold on the street with sulfonylurea compounds has been documented previously; this often presents as refractory hypoglycemia after exposure to these drugs.[6-9] Review of poison control data from 2001-2015 demonstrated that 63% of medication-mediated hypoglycemia cases involved sulfonylurea ingestion.[1] Hypoglycemia usually occurs within several hours of sulfonylurea ingestion but may persist for days and become refractory to intravenous dextrose.[4] Effects can last anywhere from six to 72 hours, depending on each individual drug's duration of action.[1] In addition to dextrose and oral nutrition, patients presenting with sulfonylurea-induced hypoglycemia should be treated with octreotide (50 to 100 mcg, subcutaneously, every six hours), which decreases insulin release from pancreatic beta cells. Several laboratories allow for testing for presence of sulfonylurea drugs in the serum or plasma, but results often take several days to come back, limiting usefulness in the immediate recognition and treatment of sulfonylurea toxicity.[10] Emergency physicians should take a thorough medication history, including both prescribed and illicit drugs, when caring for patients with undifferentiated hypoglycemia and should consider empiric octreotide if there is concern for sulfonylurea ingestion.

Limitations

This case was limited by the inability to test the composition of the offending pills, which could have confirmed whether the patient ingested glipizide pills that were substituted for oxycodone, or whether the oxycodone itself was contaminated with glipizide.

CONCLUSIONS

Refractory hypoglycemia may be due to inadvertent or intentional consumption of sulfonylurea medications. Ingestion of street drugs may present a potential source of sulfonylurea exposure and should be considered when treating patients with hypoglycemia.

References

1. Bosse GM. Chapter 47: Antidiabetics and Hypoglycemics/Antiglycemics. In: Nelson LS, Howland MA, Lewin NA, Smith SW, Goldfrank LR, Hoffman RS, *Goldfrank's Toxicology Emergencies*. 11th ed. McGraw Hill. 2019;694-706.
2. Wexler DJ, Nathan DM, Rubinow K. Sulfonylureas and meglitinides in the treatment of type 2 diabetes mellitus. In: *UpToDate*, Post TW (Ed), UpToDate, Waltham, MA. (Accessed: 15 Apr 2023).
3. McLaughlin SA, Crandall CS, McKinney PE. Octreotide: an antidote for sulfonylurea-induced hypoglycemia. Ann Emerg Med. 2000 Aug;36(2):133-138.
4. Klein-Schwartz W, Stassinos GL, Isbister GK. Treatment of sulfonylurea and insulin overdose. Br J Clin Pharmacol. 2016 Mar;81(3):496-504.
5. Chu J, Stolback A, Burns MM, Hendrickson RG, Ganetsky M. Sulfonylurea agent poisoning. In: *UpToDate*, Post TW (Ed), UpToDate, Waltham, MA. Accessed: 15 Apr 2023.
6. Peng FB, Li S. Drug Abuse Manifesting as Persistent Hypoglycemia: A Case Report of Hidden Sulfonylurea Poisoning. Presented at *Thomas Jefferson University Department of Medicine Posters* 2018, Philadelphia, PA. P12.
7. Ross JA, Downs JW, Bazydlo LA, Bordwine PH, Gineste CE, Kopatic MC, Rege SV, Saady DM, Utah OF, Wyatt SA, Wills BK,

Rose SR, Holstege C. Outbreak of Severe Hypoglycemia After Ingestion of a Male Enhancement Supplement - Virginia, August-November 2019. MMWR Morb Mortal Wkly Rep. 2020 Jun 19;69(24):740-743.

8. Narayanaswamy AKP, Williams N, Agarwal N, Okosieme O. 2012. Hypoglycaemia outbreak: a new danger on the streets? Presented at Society for Endocrinology BES 2012, Harrogate, UK. *Endocrine Abstracts*. 28, P70.
9. Chin RL. Oral hypoglycemics sold as Valium on the streets: a case report. Ann Emerg Med. 2004 Nov;44(5):552.
10. Hypoglycemia panel (sulfonylureas), serum or plasma (no date). ARUP Laboratories Test Directory. Available at: https://ltd.aruplab.com/Tests/Pub/3005636 Accessed: 15 Apr 2023.

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Common Peroneal Nerve and Tarsal Tunnel Release Surgery in an Adolescent Male with Hunter Syndrome: Illustrative Case

ELIJAH M. PERSAD-PAISLEY, BA, MD'25; BELINDA SHAO, MD, MPH; VINAY RAO, MD; LOREE K. KALLIAINEN, MD, MA

ABSTRACT

BACKGROUND: Children with Hunter syndrome have a high prevalence of nerve compression syndromes given the buildup of glycosaminoglycans in the tendon sheaths and soft tissue structures. These are often comorbid with orthopedic conditions given joint and tendon contractures due to the same pathology. While carpal tunnel syndrome and surgical treatment has been well-reported in this population, the literature on lower extremity nerve compression syndromes and their treatment in Hunter syndrome is sparse.

OBSERVATIONS: We report the case of a 13-year-old male with a history of Hunter syndrome who presented with toe-walking and tenderness over the peroneal and tarsal tunnel areas. He underwent bilateral common peroneal nerve and tarsal tunnel releases, with findings of severe nerve compression and hypertrophied soft tissue structures demonstrating fibromuscular scarring on pathology. Post-operatively, the patient's family reported subjective improvement in lower extremity mobility and plantar flexion.

LESSONS: In this case, peroneal and tarsal nerve compression were diagnosed clinically and treated effectively with surgical release and postoperative ankle casting. Given the wide differential of common comorbid orthopedic conditions in Hunter syndrome and the lack of validated electrodiagnostic normative values in this population, the history and physical examination and consideration of nerve compression syndromes are tantamount for successful workup and treatment of gait abnormalities in the child with Hunter syndrome.

KEYWORDS: Hunter syndrome, MPS II, tarsal tunnel release, peroneal nerve release

INTRODUCTION

Hunter syndrome, or mucopolysaccharidosis type II (MPS II), is a rare, X-linked inherited disorder characterized by a lack of lysosomal iduronate-2-sulfatase enzyme that results in an intracellular and extracellular accumulation of glycosaminoglycans (GAGs).[1] This buildup can damage organs and tissues throughout the body, including peripheral nerves, due to soft tissue becoming "viscous" and fascia becoming thickened.[2] Nerve compression syndromes are highly prevalent among patients with Hunter syndrome, with up to 95% of patients reported to eventually develop carpal tunnel syndrome (CTS).[3] While the literature on CTS and its surgical release in Hunter syndrome is well established,[4–9] nerve compression syndromes of the lower extremity are minimally reported. We present an illustrative case of the diagnosis and surgical treatment peroneal and tibial nerve compression syndromes with release of the common peroneal nerve and tarsal tunnel in the bilateral lower extremities.

ILLUSTRATIVE CASE

The patient is a 13-year-old male with a history of Hunter Syndrome who presented to the plastic surgery office with progressive toe-walking in an externally-rotated gait, and tenderness over the bilateral peroneal and tarsal areas. He had a strong nerve compression history, with bilateral carpal tunnel releases performed at age three, requiring repeat releases at age 11 accompanied at that time by bilateral pronator releases as well as right and middle finger trigger releases. Additional history included reactive airway disease, and intravenous and intrathecal enzyme therapy as part of a clinical trial.

On physical examination, the patient demonstrated a toe-walking gait (**Video 1**). He was only able to descend onto his heels if externally rotating his legs and then gradually internally rotating them until his toes pointed forward.

Video 1. Pre-operative gait [https://vimeo.com/915299525]

Tenderness to palpation was elicited on the outside of the leg just below the knee in the common peroneal nerve area, and on the inner ankle over the tarsal tunnel area. He held his ankles in extension, but they were able to be flexed into a neutral position, which was thought to imply that the Achilles tendons did not need to be lengthened.

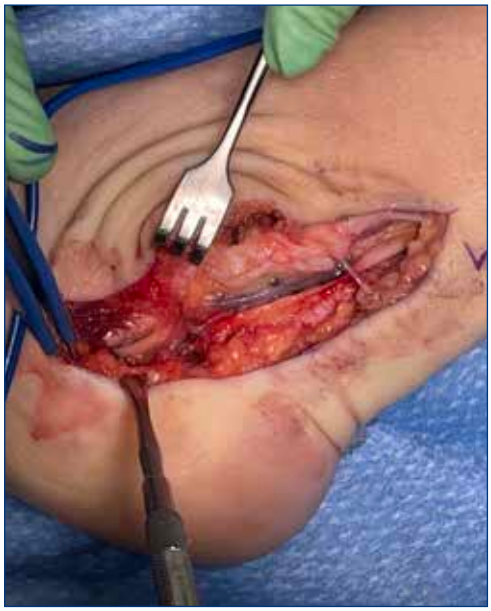
Consideration of clinical factors led to the hypothesis that peroneal nerve compression was affecting ankle extension, and that tarsal tunnel compression was causing plantar nerve irritation and pain, culminating in it being easier and less painful to walk on his toes instead of the soles of his feet. Given his robust positive response to prior nerve decompression in the upper extremities and the natural history of GAG buildup in the soft tissues, peroneal nerve and tarsal tunnel release surgeries were offered. Electrodiagnostic studies for further workup were discussed but forgone, given the strong history and physical exam findings, as well as the lack of known normative electrodiagnostic values for the lower extremity in children, let alone children with Hunter syndrome. Second opinions also offered the options of Achilles tendon lengthening and plantar fasciotomy. Ultimately, the family chose to pursue nerve decompression with post-operative casting of ankles in a neutral position.

The patient was taken to the operating room where general anesthesia was induced using a laryngeal mask airway and fiber-optic bronchoscopy confirmation given a history of difficult intubation due to macroglossia and cervical spine immobility, as well as reactive airway disease. A local direct subcutaneous block over the four incision sites was administered. Esmarch exsanguination followed by tourniquet inflation to 225 mmHg was performed.

For the common peroneal nerve releases, a curvilinear incision was made using a #15 scalpel blade on the lateral portion of the left lower extremity. The fat was dissected from the muscle using tenotomy scissors. The nerve was not readily palpable. A linear incision was made in the fascia covering the extensor digitorum longus and peroneus longus, which was noted to be extremely thickened. The nerve was identified and noted to be extremely flattened. It was dissected proximally and distally. The anterior and posterior crural intermuscular septae, the deep tendinous fascia, and the innominate intermuscular septum were incised and removed until the nerve appeared free. By the end of this decompression, the intrinsic blood vessels in the nerve became more visible as blood was able to fill them more freely as compression was released (**Figure 1**).

Figure 1. Peroneal nerve beneath the peroneus fascia

Figure 2. Tibial nerve in the tarsal tunnel



For the tarsal tunnel releases, an incision was made with a #15 blade scalpel posterior to and along the path of the posterior tibial nerve. Blunt dissection was used to preserve longitudinal crossing nerve branches. Vessels were cauterized with bipolar cautery or clipped. The nerve was identified proximal to the flexor retinaculum, and the retinaculum was divided over the nerve. The nerve was significantly flattened and pearly white/avascular appearing (**Figure 2**). In the left tarsal tunnel, inflammatory fluid was noted within the tunnel and the flexor retinaculum was severely tight. The abductor hallucis was identified. There was notable synovitis in the tarsal tunnel as well as significant compression at the foot along the undersurface of the abductor hallicus. Its fascia was divided; the muscle was retracted; and deep fascia was divided. The scissor was inserted into the medial and lateral plantar canals and the roofs were opened. The septum between the nerves was divided to create a large tunnel.

The wounds were closed with deep dermal 3-0 monocryl interrupted stitches, and a running subcuticular 4-0 monocryl for dermal and dermal-epidermal layers. Steristrips were then placed on the skin. The ankles were placed in a neutral position and casted using synthetic casting material. Post-operatively, the patient was admitted to a floor level of care for one night of observation. At his two-week follow up appointment, he was able to ambulate with improved plantarflexion compared to baseline (**Video 2**). Histopathology of the hypertrophied fascia demonstrated fibromuscular tissue scarring. The patient has since received routine physical therapy services.

Video 2. Post-operative gait [https://vimeo.com/915297064]

DISCUSSION

Observations

We report the case of a 13-year-old male with Hunter syndrome who developed progressive toe-walking and tenderness over the peroneal and tarsal areas, successfully treated with bilateral common peroneal nerve and tarsal tunnel releases, during which severe nerve compression and hypertrophied soft tissue structures were encountered. Several orthopedic manifestations have been identified in patients with Hunter syndrome.[10,11] However, conditions such as tarsal tunnel syndrome are infrequently reported in this patient population.[12]

Lessons

Musculoskeletal manifestations of Hunter syndrome primarily consist of spinal conditions (e.g., cervical stenosis), hip dysplasia, and, most commonly, carpal tunnel syndrome (CTS).[12,13] While CTS is highly prevalent in other MPS subtypes (e.g., Hurler, Maroteaux-Lamy syndrome), other nerve entrapment syndromes, such as tarsal tunnel syndrome (TTS), occur less commonly in among these patients.[12]

In their 2019 case series of 19 MPS patients, Williams et al report mixed results in the diagnosis and post-operative outcomes of four patients (two with MPS I, two with MPS VI) with a suspected diagnosis of TTS.[12] One patient with MPS VI was clinically diagnosed with TTS and experienced symptom relief following bilateral tarsal tunnel decompressions. Two patients had inconclusive nerve conduction studies but had resolution of lower extremity pain following tarsal tunnel decompression for one patient (MPS VI) and spinal fusion for the other (MPS I). The final patient with MPS I had inconclusive lower extremity nerve conduction studies but underwent tarsal tunnel release with subsequent pain resolution post-operatively. These findings indicate mixed results in the clinical and electromyographical diagnosis of patients with MPS, and variable yet promising results following nerve decompression surgery.

In this case, peroneal and tarsal nerve compression were diagnosed clinically and treated effectively with surgical release and postoperative ankle casting. Given the wide differential of common comorbid orthopedic conditions in Hunter syndrome and the lack of validated electrodiagnostic normative values in this population, the history and physical examination and consideration of nerve compression syndromes are valuable for successful workup and treatment of gait abnormalities in a child with Hunter syndrome. Furthermore, communication barriers in patients with Hunter syndrome may limit symptom reporting, and subtle signs of nerve compression may be overlooked by higher acuity medical conditions, thereby putting this population at increased risk of more advanced disease at the time of diagnosis.[3]

Limitations

This is a single case report of a rare disease case and therefore does not intend to provide a high level of evidence to inform treatment decisions.

CONCLUSION

In this case of a 13-year-old male with Hunter syndrome, peroneal and tarsal nerve compression were diagnosed clinically and treated effectively with surgical release and postoperative ankle casting. Given the wide differential of common comorbid orthopedic conditions in Hunter syndrome and the lack of validated electrodiagnostic normative values in this population, the history and physical examination and consideration of nerve compression syndromes are tantamount for successful workup and treatment of gait abnormalities in the child with Hunter syndrome.

References

1. Hashmi MS, Gupta V. Mucopolysaccharidosis Type II. In: *StatPearls*. StatPearls Publishing; 2023. Accessed July 18, 2023. http://www.ncbi.nlm.nih.gov/books/NBK560829/
2. Stapleton M, Kubaski F, Mason RW, et al. Presentation and Treatments for Mucopolysaccharidosis Type II (MPS II; Hunter Syndrome). *Expert Opin Orphan Drugs*. 2017;5(4):295-307. doi:10.1080/21678707.2017.1296761
3. Argenta AE, Davit A. Carpal Tunnel Syndrome in the Setting of Mucopolysaccharidosis II (Hunter Syndrome). *Plast Reconstr Surg Glob Open*. 2017;5(8):e1477. doi:10.1097/GOX.0000000000001477
4. Wraith JE, Alani SM. Carpal tunnel syndrome in the mucopolysaccharidoses and related disorders. *Arch Dis Child*. 1990;65(9):962-963. doi:10.1136/adc.65.9.962
5. Norman-Taylor F, Fixsen JA, Sharrard WJ. Hunter's syndrome as a cause of childhood carpal tunnel syndrome: a report of three cases. *J Pediatr Orthop B*. 1995;4(1):106-109. doi:10.1097/01202412-199504010-00018
6. Haddad FS, Jones DH, Vellodi A, Kane N, Pitt MC. Carpal tunnel syndrome in the mucopolysaccharidoses and mucolipidoses. *J Bone Joint Surg Br*. 1997;79(4):576-582. doi:10.1302/0301-620x.79b4.7547
7. Van Heest AE, House J, Krivit W, Walker K. Surgical treatment of carpal tunnel syndrome and trigger digits in children with mucopolysaccharide storage disorders. *J Hand Surg Am*. 1998;23(2):236-243. doi:10.1016/S0363-5023(98)80120-2

8. Yuen A, Dowling G, Johnstone B, Kornberg A, Coombs C. Carpal tunnel syndrome in children with mucopolysaccaridoses. *J Child Neurol*. 2007;22(3):260-263. doi:10.1177/0883073807300528
9. Jadhav T, Kornberg AJ, Peters H, Lee J, Ryan MM. Carpal tunnel syndrome in pediatric mucopolysaccharidoses. *Clinical Neurophysiology*. 2014;125(4):e4-e5. doi:10.1016/j.clinph.2013.10.033
10. Link B, de Camargo Pinto LL, Giugliani R, et al. Orthopedic manifestations in patients with mucopolysaccharidosis type II (Hunter syndrome) enrolled in the Hunter Outcome Survey. *Orthop Rev (Pavia)*. 2010;2(2):e16. doi:10.4081/or.2010.e16
11. Link B, Botha J, Giugliani R. Characterization of orthopedic manifestations in patients with mucopolysaccharidosis II using data from 15 years of the Hunter Outcome Survey. *JIMD Rep*. 2023;65(1):17-24. doi:10.1002/jmd2.12401
12. Williams N, Willet J, Clark D, Ketteridge D. Tarsal tunnel syndrome in the mucopolysaccharidoses: A case series and literature review. *JIMD Rep*. 2019;46(1):16-22. doi:10.1002/jmd2.12021
13. Stepien KM, Bentley A, Chen C, et al. Non-cardiac Manifestations in Adult Patients with Mucopolysaccharidosis. *Frontiers in Cardiovascular Medicine*. 2022;9. Accessed July 24, 2023. https://www.frontiersin.org/articles/10.3389/fcvm.2022.839391

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A Consequence of an Electrical-Burn Injury: Atrial Fibrillation

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ABSTRACT

Cardiac arrhythmias following electrocution injuries can accompany high-voltage or high- intensity currents. Contributing factors to electrical hazard are the type of current, voltage, resistance, and duration of contact and pathway through the body. It is important to monitor for delayed arrhythmias in patients with an electrical injury. We describe a case of a 52-year-old man who presented after an electrical shock injury while grabbing a 5,000-voltage wire at work. In this case report, we discuss the presentation, management, and follow-up recommendations for this type of injury.

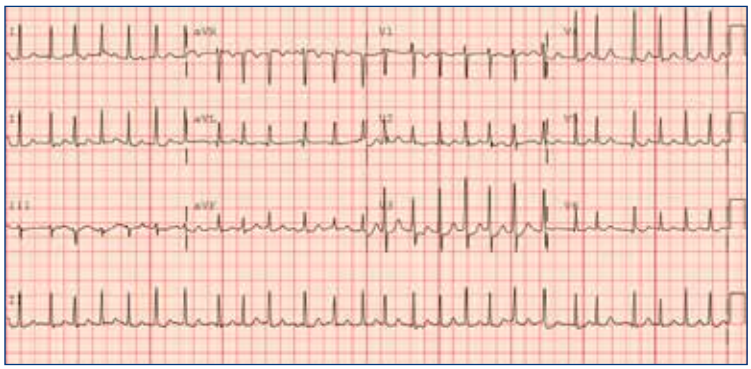
KEYWORDS: arrhythmia, electrocution injuries, trauma

CASE PRESENTATION AND SUMMARY

A 52-year-old male electrician with a history of uncomplicated rheumatic fever and no cardiac medical history presented to the Emergency Department after sustaining an electrical shock injury while grabbing a high-voltage electrical wire. The patient was working at the local airport and arrived to the Emergency Department approximately 20 minutes after making contact with a wire at work with both hands and experiencing 5,000 V that traveled from his left hand to his right hand. He reported holding on to the wire for approximately 15 seconds and then letting go and falling directly onto his face. There was no reported loss of consciousness. He stated he felt his heart racing. The patient denied any associated symptoms of chest pain, diaphoresis, nausea, or vomiting prior to arrival. His social history was significant for drinking several beers per day, but he had no history of a withdrawal. He is a non-smoker. Given his history of childhood rheumatic fever without carditis, he had undergone multiple surveillance echocardiograms, the last of which was eight years ago.

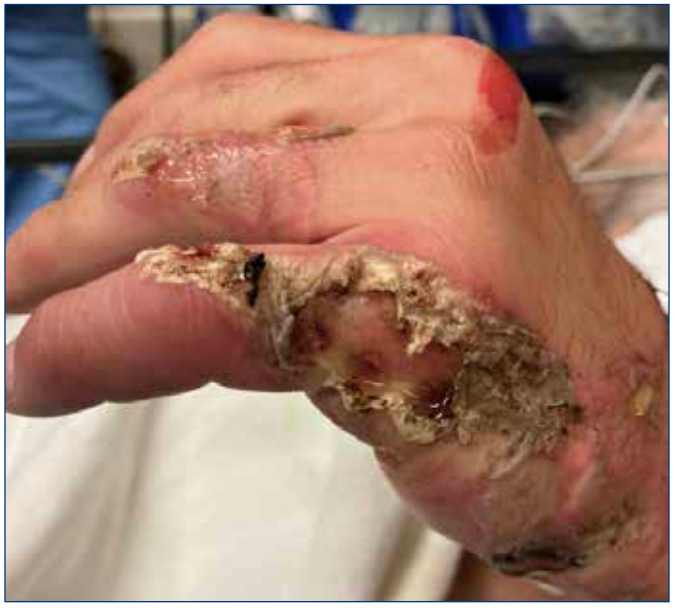
Lab work performed included complete blood count (CBC), basic metabolic panel (BMP), liver function tests (LFTs), all of which were within normal limits. The patient had a normal creatine kinase (CK), and his urinalysis (UA) did not show myoglobinuria. His initial high sensitivity troponin was < 3 ng/L (ref: 3–57 ng/L), and his initial EKG revealed atrial fibrillation with a rapid ventricular rate (RVR) in the 150s–160s

Image 1. Patient's presenting EKG (atrial fibrillation with rapid ventricular response)



(**Image 1**). Point-of-care ultrasound (POCUS) echocardiography performed by the ED provider was limited, but a grossly normal ejection fraction was appreciated, and no pericardial effusion was detected. The patient sustained bilateral hand burns with deep burn at the first webspace of the left hand (**Image 2**). The patient had several abrasions and lacerations to his face that were repaired.

Image 2. Patient's electrocution burns on presentation to the Emergency Department



A computed tomography (CT) scan of his head, cervical spine, face, chest, abdomen and pelvis was performed given the significant mechanism of injury. CT imaging was remarkable only for a nasal bone fracture. Atrial fibrillation with RVR was treated with two doses of metoprolol 5mg intravenously (IV), followed by the initiation of a diltiazem drip with a heart rate goal of <120 BPM. He was admitted to the trauma intensive care unit (TICU) due to the severity of his burns and the persistent rapid ventricular rate. He was further treated with amiodarone 150mg IV in the TICU, as the inpatient team aimed to obtain rhythm control in addition to rate control.

DISCUSSION

Electrical burns account for 4–5% of all burns treated in a medical setting.[1] While there has been improvement in injury prevention and implementation of safety protocols at the workplace, electrical injuries in the adult population are most often work-related and are the fourth leading cause of traumatic work-related death in the United States, with approximately 1,000 work-related deaths occurring annually.[2,3] Accidental high-voltage electrical injuries comprise approximately 400 of these cases.[1] Despite the rarity of electrical injuries, the morbidity and mortality are high – ranging from 10–30% – and it is imperative to obtain the voltage of injury from the patient or their workplace upon arrival to the Emergency Department.[4]

The magnitude of electrical hazard is dependent on multiple factors, including voltage (V), resistance (R), type of current (alternating or direct), duration of contact, and the path that the electricity takes throughout the body.[5,6] Current intensity (I), which is measured in Amperes (A), contributes to the severity of the electrical injury. This considers both voltage and resistance as described by Ohm's law [I=V/R]. While there are variable definitions of voltage magnitude in the literature, it is generally accepted that <600 V is low and >1000 V is high.[2,7,8] The difference between Alternating Current (AC) and Direct Current (DC) is important to consider as well. In AC the direction of flow of electrons changes on a cyclical basis, whereas in DC the direction of flow remains constant. Common household breakers range between 15–20 A, and the threshold for ventricular fibrillation is as little as 50–100mA, demonstrating the possible danger of domestic electrical injury. AC is thought to be about 3-5 times more damaging than DC. This is because AC can induce muscle tetany due to strong muscle contractions, which does not allow a person to easily let go of an electrical source.[2] The patient in this case report described this sensation on presentation. He felt that his hands were "stuck" holding onto the wire. Electrical energy, which is converted into thermal energy, lead to the burns on our patient's hand (**Image 2**). This occurs, in part, due to the body becoming part of the circuit.[2]

High-voltage injuries, as seen in our patient, should be treated as multi-system trauma. High-voltage electrical injuries generally have significantly greater morbidity as seen by larger numbers of surgical procedures required, higher rates of medical complications, and multiple post-traumatic injuries secondary to additional falls in these injuries.[8] While low voltage is associated with fewer fatalities, low-voltage AC injuries are particularly arrhythmogenic and can cause ventricular dysrhythmias.[8]

The exact rate of dysrhythmias following an electrical injury is unknown.[4] The most common arrhythmias described in the literature include sinus tachycardia, premature ventricular contractions (PVCs), premature atrial contractions (PACs), and sinus bradycardia.[4] However, cases of supraventricular tachycardia, atrial fibrillation, ventricular tachycardia, ventricular fibrillation, and asystole have been documented as possible sequelae of electrical injury. The majority of arrhythmias occur shortly after the electrical shock and, more rarely, there are delayed ventricular arrhythmias. The most common fatal dysrhythmia is ventricular fibrillation. Asystole is associated with lightning or high-voltage injuries.[4,8-13] Other arrhythmias that occur include first- and second-degree AV block and bundle branch blocks.[13]

While the pathophysiology of these arrhythmias is not well understood, it is thought that the development of an arrhythmia may occur due to changes in extracellular potassium concentration, an increased Na+/K+ pump concentration, and may be associated with transient and localized changes in sodium and potassium transport, potassium concentration, and membrane potential. This is proposed to lead to enhanced automaticity of the myocardium.[9]

Although most arrhythmias can be diagnosed on initial EKG, there have also been case reports of delayed arrhythmias reported in the literature.[12,13,14] A striking case reported by Sharma et al described a 24-year-old male who sustained a 220–240V electrical injury in his home. On arrival at the hospital, he was found to have first-degree heart block which, over the next 24 hours, deteriorated into Mobitz type 1 heart block, complete heart block, and then eventually ventricular fibrillation requiring electrical cardioversion.[14] Karatas et al reported a patient who developed pulseless ventricular tachycardia within 24 hours of hospitalization, which ultimately was terminated with DC shock.[15] More recent systematic reviews suggest that clinically relevant arrythmias not noted on initial presentation to the hospital are rare in patients after an electrical accident, and that clinically relevant arrhythmias are likely to be diagnosed on presenting EKG.[10,16-18]

Due to the high incidence of dysrhythmia, autonomic dysfunction, and delay in presentation of a fatal arrhythmia, current recommendations suggest continuous cardiac monitoring for >24 hours for all patients except those who sustain low-voltage shocks, are asymptomatic, have no loss of

consciousness, and have a completely normal physical exam, including a normal skin exam without burns. For patients with high-voltage injuries, and who have EKG abnormalities, loss of consciousness, or have cardiac risk factors, 24 hours of cardiac monitoring is indicated.[17] Because troponin is specific to the cardiac muscle, it seems reasonable to monitor patients with an elevated troponin, though there have not been specific studies looking at troponin increase in these settings.[1] Elevations in creatinine kinase on the other hand may be confounded with peripheral skeletal muscle injury, which are common in electrocution.

Atrial fibrillation after an electrocution injury is uncommon.[19] The management of atrial fibrillation with RVR secondary to electrical injury follows standard treatment guidelines and requires a combination of rhythm and rate control. Our patient's rhythm converted into normal sinus rhythm 12 hours after he arrived to the hospital. An inpatient echocardiogram demonstrated mild pulmonary hypertension and elevated right-sided filling pressures, but demonstrated no cardiac wall motion abnormalities or pericardial effusion. He did not have recurrence of his atrial fibrillation during his hospitalization and was discharged several days later. He was not started on any rate or rhythm controlling medications on discharge, nor was he started on anticoagulation medications. During a follow-up cardiology appointment one month after discharge, he was noted to be in normal sinus rhythm and was without any cardiac sequelae.

References

1. Gentges J, Schieche C. Electrical injuries in the emergency department: an evidence-based review. Emerg Med Pract. 2018 Nov;20(11):1-20.
2. Bounds EJ, Khan M, Kok SJ. Electrical Burns. [Updated 2023 April 24]. In:StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK519514/
3. Brandão C, Vaz M, Brito IM, Ferreira B, Meireles R, Ramos S, Cabral L. Electrical burns: a retrospective analysis over a 10-year period. Ann Burns Fire Disasters. 2017 Dec 31;30(4):268-271.
4. Pilecky D, Vamos M, Bogyi P, Muk B, Stauder D, Racz H, Nyolczas N, Duray GZ, Zacher G, Zima E. Risk of cardiac arrhythmias after electrical accident: a single-center study of 480 patients. Clin Res Cardiol. 2019 Aug;108(8):901-908. doi: 10.1007/s00392-019-01420-2. Epub 2019 Feb 15. PMID: 30771067; PMCID: PMC6652167.
5. Lee RC, Zhang D, Hannig J. Biophysical injury mechanisms in electrical shock trauma. Annu Rev Biomed Eng. 2000;2:477-509. doi: 10.1146/annurev.bioeng.2.1.477. PMID: 11701521.
6. Arnoldo BD, Purdue GF. The diagnosis and management of electrical injuries. Hand Clin. 2009 Nov;25(4):469-79. doi: 10.1016/j.hcl.2009.06.001. PMID: 19801121.
7. Daskal Y, Beicker A, Dudkiewicz M, Kessel B. [High Voltage Electric Injury: Mechanism of Injury, Clinical Features and Initial Evaluation.]. Harefuah. 2019 Jan;158(1):65-69. Hebrew. PMID: 30663297.
8. Shih JG, Shahrokhi S, Jeschke MG. Review of Adult Electrical Burn Injury Outcomes Worldwide: An Analysis of Low-Voltage vs High-Voltage Electrical Injury. J Burn Care Res. 2017 Jan/Feb;38(1):e293-e298. doi: 10.1097/BCR.0000000000000373. PMID: 27359191; PMCID: PMC5179293.
9. Waldmann V, Narayanan K, Combes N, Jost D, Jouven X, Marijon E. Electrical cardiac injuries: current concepts and management, European Heart Journal. 21 April 2018;39(16):1459–1465. https://doi.org/10.1093/eurheartj/ehx142
10. Pawlik AM, Lampart A, Stephan FP, Bingisser R, Ummenhofer W, Nickel CH. Outcomes of electrical injuries in the emergency department: a 10-year retrospective study. Eur J Emerg Med. 2015;23:448–454.
11. Alhazmi L. Reversibility of Sinus Bradycardia-Induced Syncope Resulting From Low-Voltage Electrical Injury: A Case Report. Cureus. 2023 Dec 14;15(12):e50509. doi: 10.7759/cureus.50509. PMID: 38222168; PMCID: PMC10787379.
12. Akkaş M, Hocagil H, Ay D, Erbil B, Kunt MM, Ozmen MM. Cardiac monitoring in patients with electrocution injury. Ulus Travma Acil Cerrahi Derg. 2012 Jul;18(4):301-5. doi: 10.5505/tjtes.2012.69158. PMID: 23138995.
13. Yew KL. Electrocution-induced symptomatic bradycardia necessitating pacemaker implantation. Heart Views. 2014 Apr;15(2):49-50. doi: 10.4103/1995-705X.137497. PMID: 25104983; PMCID: PMC4124666.
14. Sharma BC, PatialRK, Pal LS, SaunkhlaJ, Thakur SS (1990) Electrocardiographic manifestations following household electric current injury. J Assoc Physicians India. 38(12):938–939.
15. Karataş MB, Onuk T, Güngör B, et al. Assessment of electrocardiographic parameters in patients with electrocution injury. J Electrocardiol. 2015;48(5):809–814. doi: 10.1016/j.jelectrocard.2015.06.009
16. Hansen SM, Riahi S, Hjortshoj S, et al. Mortality and risk of cardiac complications among immediate survivors of accidental electric shock: a Danish nationwide cohort study. BMJ Open. 2017;7(8):e015967. doi: 10.1136/bmjopen-2017-015967.
17. Bailey B, Gaudreault P, Thivierge RL. Cardiac monitoring of high-risk patients after an electrical injury: a prospective multicentre study. Emerg Med J. 2007;24(5):348–352. doi: 10.1136/emj.2006.044677.
18. Searle J, Slagman A, Maass W, Mockel M. Cardiac monitoring in patients with electrical injuries. An analysis of 268 patients at the Charite Hospital. Dtsch Arztebl Int. 2013;110(50):847–853.
19. Bilik M, Akyüz A, Akıl M, İnci U, Acet H, Toprak N. Unexpected guest: Atrial fibrillation due to electrical shock, International Journal of the Cardiovascular Academy. 2016;2(1):40-41. ISSN 2405-8181, https://doi.org/10.1016/j.ijcac.2016.02.001.

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Ebstein's Anomaly of the Tricuspid Valve

BEATRIZ RIZKALLAH ALVES, MD; CAROLINA SALDANHA NEVES HORTA LIMA, MD; SOMWAIL RASLA, MD

A 27-year-old female presented with three months of palpitations and chest pain. Upon cardiac auscultation, a 3/6 systolic murmur could be heard at the left lower sternal border followed by a loud S3. The systolic murmur increased during inspiration; and no diastolic murmur was appreciated. The electrocardiogram revealed sinus rhythm, right bundle branch block and right-axis-deviation (**Figure 1A**). A 15-day cardiac monitoring demonstrated only rare premature ventricular contractions. A chest radiograph performed during the initial visit demonstrated an enlarged right heart silhouette, a rectified left heart border due to a displaced and dilated right ventricle and a small ascending aortic knob (**Figure 1B**), A transthoracic echo (**Figure 1C**) revealed severely dilated right heart chambers, decreased right ventricular systolic function and an apically displaced septal leaflet of the tricuspid valve with

Figure 1A. Electrocardiogram revealing right bundle branch block and heart axis deviation to the right.

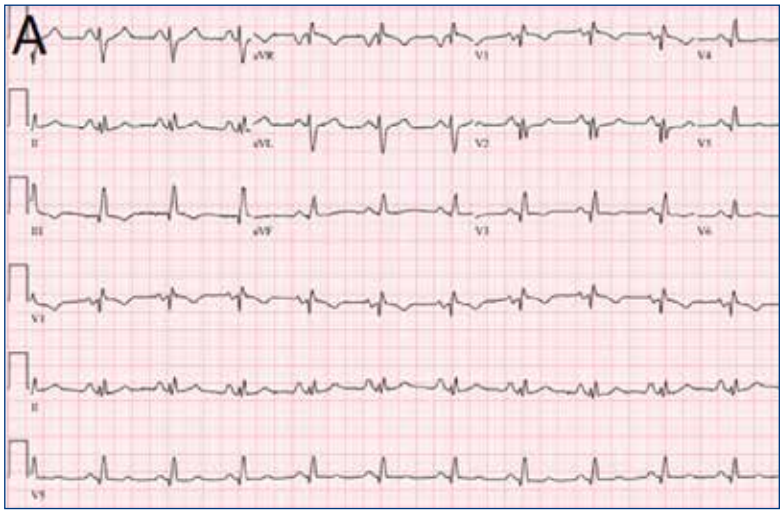


Figure 1B: Chest radiograph

Chest radiograph demonstrates an enlarged right atrium making up the entire right heart border (1), straightening of the left heart border (2) and a small ascending aortic knob (3). The cardiac silhouette is also enlarged with a cardiothoracic ratio greater than 50% on a PA view of the chest (4).

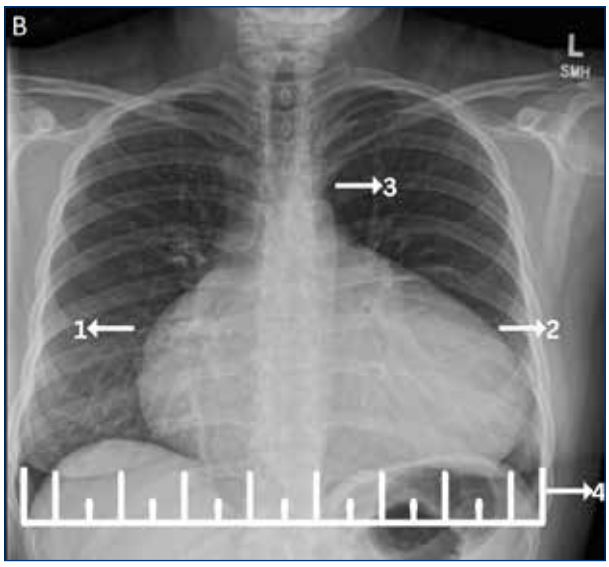


Figure 1C: Transthoracic Echocardiogram

Transthoracic echocardiogram showed a markedly dilated right atrium with an "atrialized" right ventricle and apical displacement of the septal leaflet of the tricuspid valve, characteristic of Ebstein's anomaly. In addition, there was a small left ventricle (LV) and left atrium (LA) with a flattened interventricular septum, suggesting pressure and volume overload. No other congenital abnormalities were identified.

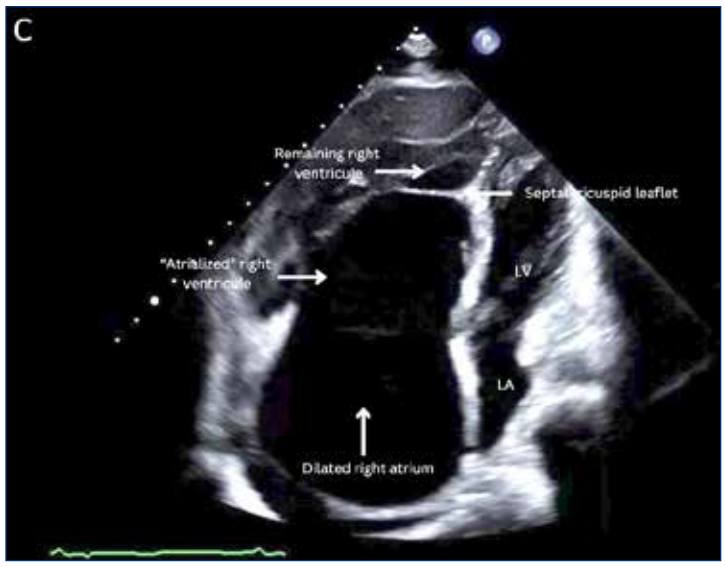
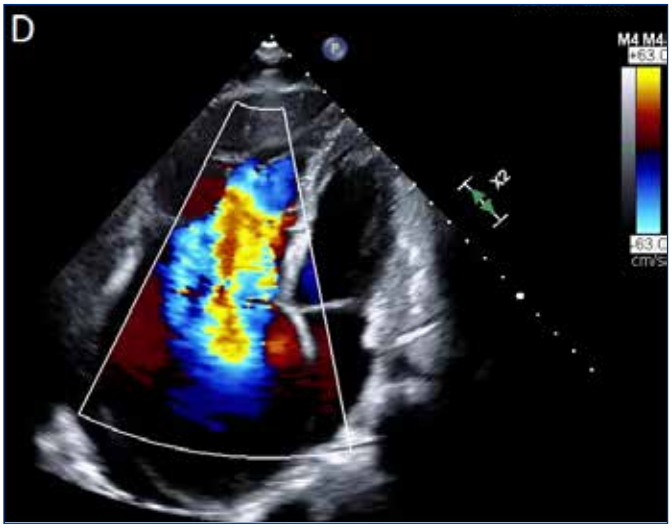


Figure 1D. Transthoracic Echocardiogram – doppler of tricuspid valve
Doppler of the tricuspid valve revealed severe tricuspid regurgitation.



"atrialization" of the right ventricle. There was severe tricuspid valve regurgitation (**Figure 1D**), also seen on cardiac MRI, which confirmed regurgitant fraction of 78%, but no evidence of intracardiac shunting. Finally, for functional capacity evaluation, the patient underwent cardiopulmonary exercise testing which was non-diagnostic for ischemia due to failure to achieve 85% of age-predicted maximum heart rate likely in the setting of betablocker therapy started before the study. The test demonstrated impaired exercise capacity based on peak VO2 of 19.2 ml/kg/min (47% predicted). Surprisingly, our patient lived almost three decades without any major symptoms that would have precipitated prior investigation.

Despite the significant anatomic disruption seen in the images, she presented clinically with no overt signs or symptoms of heart failure. After shared decision making, patient was managed conservatively with betablockers for symptom control. She was referred to cardiothoracic surgery for close surveillance of any changes in clinical status that would warrant anatomic correction.

This constellation of findings is consistent with Ebstein's anomaly; a congenital malformation of the tricuspid valve with a wide spectrum of presentations depending on the degree of anatomic disruption. Patients with minimally displaced leaflets, or less impaired ventricular function, may develop appropriately until adulthood and remain asymptomatic or only mildly symptomatic. In contrast, the disease may also manifest with severe cardiomegaly (often seen in a routine anteroposterior chest radiograph), right heart failure, pulmonary hypoplasia or even intracardiac shunts. The impact of such severe pathophysiologic changes translates into the high rates of perinatal morbidity and mortality in the affected population. In addition, conduction diseases such as accessory pathways and Wolf-Parkinson-White are strongly associated with Ebstein's anomaly, potentially leading to malignant arrhythmias and sudden cardiac death.

Finally, regarding treatment strategies, the approach may vary from symptom relief therapy, aiming for right ventricle unload, to anatomic correction. Surgery is warranted for high degrees of tricuspid regurgitation and right heart failure, severe pulmonary hypertension, intra-cardiac shunts leading to persistent hypoxemia and cyanosis or uncontrolled arrythmias. A negative impact in functionality may also qualify patients for surgical repair, especially considering that most of these individuals are children or young adults at risk for impaired development or limited lifestyle. Pacemakers or implantable cardiac defibrillators might also be indicated to manage or prevent life threatening arrhythmias.

In summary, Ebstein's anomaly is a congenital disease of the tricuspid valve and right heart that can present with a myriad of signs and symptoms. Diagnosis is usually made in the early stages of life prompting surgical correction, or, alternatively, requiring aggressive clinical treatment to ensure a healthy development and lifestyle. Multidisciplinary team and specialized services are also fundamental to provide optimal care and surveillance, mitigating further complications and high rates of mortality.

References

1. Attenhofer Jost CH, Connolly HM, Dearani JA, Edwards WD, Danielson GK. Ebstein's anomaly. Circulation. 2007 Jan 16;115(2):277–85.
2. Celermajer DS, Bull C, Till JA, et al. Ebstein's anomaly: presentation and outcome from fetus to adult. J Am Coll Cardiol. 1994;23:170.
3. Zuberbuhler JR, Allwork SP, Anderson RH. The spectrum of Ebstein's anomaly of the tricuspid valve. J Thorac Cardiovasc Surg. 1979;77:202–211.

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Disclaimer

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Upper-Extremity Klippel-Trenaunay Syndrome

SYED BUKHARI, MD; AMMAR SAATI, MD

A 26-year-old woman presented for evaluation of cutaneous pigmentation involving the left upper extremity, left breast, and left upper back since birth. She had developed chronic swelling of her left upper extremity during childhood, and began to notice visible veins. She was asymptomatic due to which medical attention was not sought in the past, but now she was curious to know about it. Physical examination revealed massive lymphedema of the left upper extremity, extensive vascular hemangioma of 'port-wine' variety and varicose veins (**Figures 1A, B**). Based on the clinical presentation, as well as the triad of cutaneous port-wine capillary malformations, hemihypertrophy of bone and soft tissues, and varicose veins, the diagnosis of Klippel-Trenaunay syndrome (KTS) was established.

Figures 1A,B. Port-wine stain in the left upper extremity, extending from upper arm to the posterior aspect of the hand. Additionally, left upper extremity is more swollen compared with the contralateral limb, suggestive of hemihypertrophy of the bone and/or soft tissue.

KTS is a complex congenital anomaly that has three main components: cutaneous port-wine capillary malformations, hemihypertrophy of bone and soft tissues, and venous malformations.[1] KTS is a clinical diagnosis, and while it is a very rare condition, upper-extremity KTS is even more unusual. It is usually sporadic with an estimated incidence of 2–5 per 100,000 without any gender predilection.[2] KTS is considered a part of PIK3CA-Related Overgrowth Spectrum (PROS) – a group of clinically overlapping disorders.[3] Although the exact etiology of this spectrum remains unclear, it is thought to be secondary to abnormality of mesodermal tissues in embryologic development, caused by somatic mutations in the phosphatidylinositol-4-5-bisphosphate 3 kinase, catalytic subunit (PIK3CA) gene.[3] This results in the activation of phosphatidylinositol-3-kinase (PI3K)/protein kinase and cell overgrowth through dysregulation of the mTORC2 pathway.[3] While patients may be asymptomatic in the first few decades of their lives, rectal bleeding and/or intermittent painless hematuria are often the first clinical manifestation, and hemangiomas and varicose veins are primarily the cause of bleeding. Ironically, extensive varicosities make these patients more prone to the development of venous thromboembolism as well, and IVC filter implantation is appropriate when recurrent bleeding precludes anticoagulation use.

A multidisciplinary approach is the key for management of these patients. Although symptomatic care remains the mainstay treatment, low-dose sirolimus can provide some benefit by inhibiting growth-promoting actions of PI3K, resulting in modest reduction in overgrowth.[4] Finally, the emergence of novel targeted therapies including the recently FDA-approved PI3K pathway inhibitor, Alpelisib, has further underscored the importance of genetic testing in KTS.[5]

References

1. Alwalid O, Makamure J, Cheng QG, et al. Radiological Aspect of Klippel-Trénaunay Syndrome: A Case Series With Review of Literature. Curr Med Sci. 2018;38:925-931.
2. Iriarte Fuster A, Cerdà Serra P, Riera-Mestre A. PIK3CA-related overgrowth spectrum (PROS): new insight in known diseases. Med Clin (Barc). 2021;157:483-488.
3. Vahidnezhad H, Youssefian L, Uitto J. Klippel-Trenaunay syndrome belongs to the PIK3CA-related overgrowth spectrum (PROS). Exp Dermatol. 2016;25:17-9.
4. Parker VER, Keppler-Noreuil KM, Faivre L, et al. Safety and efficacy of low-dose sirolimus in the PIK3CA-related overgrowth spectrum. Genet Med. 2019;21:1189-1198.
5. Canaud G, Lopez Gutierrez JC, Irvine AD, et al. Alpelisib for treatment of patients with PIK3CA-related overgrowth spectrum (PROS). Genet Med. 2023;25:100969

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Urothelial Carcinoma: Epidemiology and Imaging-Based Review

ASHWIN C. REDDY, BS; JOEY Z. GU, MD; BRANDON H. KOO, MD; VICTORIA FRUH, PhD; ALESSANDRA J. SAX, MD

ABSTRACT

Bladder cancer is the 6th most common malignancy in the United States, with urothelial carcinomas comprising over 95% of cases of bladder cancer, and commands a significant disease burden in Rhode Island. Imaging studies can provide valuable diagnostic information for urothelial carcinomas at initial presentation and are routinely used for noninvasive staging, treatment response monitoring, and post-treatment surveillance. This review aims to discuss and highlight three imaging modalities: ultrasonography, computed tomography, and magnetic resonance imaging, with particular focus on the notable features and appearance of urothelial carcinoma on each modality and their relative utility throughout the disease course. A general overview of disease epidemiology and treatment practices is also provided.

KEYWORDS: Bladder cancer, urothelial carcinoma, imaging, MRI, CT

INTRODUCTION

Bladder cancer remains a significant contributor to morbidity and mortality, representing the 6th most common malignancy in the United States.[1] An estimated 82,290 new cases of bladder cancer will be diagnosed in 2023 in the United States with an estimated 16,710 deaths resulting from bladder cancer over this period.[2]

Urothelial carcinoma is the predominant histological subtype, comprising upwards of 95% of cases in the United States, and tends to be less aggressive than non-urothelial bladder carcinomas which are more commonly found in regions where Schistosoma is endemic.[3] The presence of histologic variants in urothelial carcinoma is associated with increased risk of progression.[4]

The strongest risk factor for bladder cancer development is advanced age, with a median age at diagnosis of 73 years.[2,5] Male sex is another important risk factor, with men being diagnosed with bladder cancer about four times as frequently as women, which may be explained by differences in exposures and lifestyle as well as urinary retention due to prostate enlargement and resulting stasis of urine-containing carcinogens.[6] Females typically present with more advanced disease and inferior outcomes, including increased rates of recurrence and reduced overall survival, which is commonly attributed to delays in diagnosis from lack of recognition and appropriate imaging at the time of first presenting symptoms.[7,8] Non-Hispanic White persons have the highest age-adjusted incidence of bladder cancer while Black persons have worse disease-specific outcomes which may be explained by differences in access to treatment and care.[7]

Cigarette smoking is the principal modifiable risk factor, accounting for approximately 50% of cases.[9] One meta-analysis of 89 observational studies found that smokers had over three times the risk of bladder cancer compared to never smokers and nearly two times the risk compared to former smokers.[10] While smoking exposures may be complex, it appears that the higher the cumulative smoking exposure, the higher the risk of developing bladder cancer.[11] Occupational and environmental exposures, particularly to aromatic amines and benzenes, account for approximately 10% of bladder cancer cases.[9] Chronic bladder inflammation, either through recurrent UTIs or chronic bladder catheterization, may also increase the risk of developing bladder cancer.[12,13] It has been established that diabetes mellitus is associated with an increased risk of bladder cancer, particularly in men, and recent analyses have also found an association between metabolic syndrome and bladder cancer as well.[14,15]

Genetic syndromes, most notably Lynch syndrome, may also confer increased risk of developing bladder cancer due to mutations in DNA damage repair genes, with up to 21% of patients found to have pathogenic germline variants.[9] The most common pathogenic germline variants in targeted sequencing studies are *MSH2*, *MLH1*, *BRCA1*, *BRCA2*, and *ATM*, with 18.6% of patients in the largest study harboring an actionable variant with preventive or therapeutic utility.[16]

According to statewide data obtained from the Rhode Island Cancer Registry, in Rhode Island, males were about three times as likely as females to be diagnosed with urothelial carcinoma from the period of 1995 to 2019 compared to male predominance, at a rate of about four times as likely nationally (**Table 1**). Rhode Islanders who were diagnosed with urothelial carcinoma over this period were also more likely to identify as White compared with national rates (perhaps reflecting overall racial and ethnic distributions or cancer disparities), though the overall incidence of urothelial carcinoma has decreased in Rhode Island in line with national trends.[1,2]

Table 1. Demographics and age-adjusted incidence rate of urothelial carcinoma (ICD-O-3 8120/2-3) in RI (1995–2019)

Demographics	Mean Age (years)	Male (%)	White (%)		
Urothelial carcinoma in situ (8120/2)	71.80 ± 11.05	75.44	97.81		
Urothelial carcinoma (8120/3)	72.81 ± 11.60	73.18	97.16		
Incidence (Age-adjusted incidence rate, per 100,000 individuals)	**1995–1999**	**2000–2004**	**2005–2009**	**2010–2014**	**2015–2019**
Urothelial carcinoma in situ (8120/2)	1.47	1.31	1.52	1.69	1.30
Urothelial carcinoma (8120/3)	5.94	5.35	5.60	4.92	4.08

Source: Rhode Island Cancer Registry

The most common presentation of bladder cancer is gross or microscopic hematuria. The risk of bladder cancer in a patient with gross hematuria is greater than in one with microscopic hematuria, found in one study to be 18.9% with gross hematuria compared to 4.8% with microscopic hematuria.[17] Other presentations include irritation while voiding, reduced bladder capacity, or incidental discovery on imaging. Less common presentations include urinary tract infection or upper-tract obstruction or pain with more advanced lesions.

According to the 2023 National Comprehensive Cancer Network (NCCN) guidelines on bladder cancer, there are three categories that bladder cancer can be divided into clinically based on differences in prognosis, management, and therapeutic aims: non-muscle invasive bladder cancer (NMIBC), muscle invasive bladder cancer (MIBC), and metastatic disease.[18] Visualization of the bladder is critical to the staging (using the TNM system) and management of bladder cancer, and is often done directly with cystoscopy as the gold standard for detection of bladder cancer.[18] Imaging studies are often performed at the time of initial presentation – radiologic evaluation can provide key diagnostic information and can be useful for noninvasive staging and post-treatment surveillance, particularly in higher risk patients. Here we discuss the relative utility of three imaging modalities (ultrasonography, computed tomography, and MRI) in the assessment and management of bladder cancer as well as the associated imaging features of bladder cancer in each modality.

IMAGING FEATURES

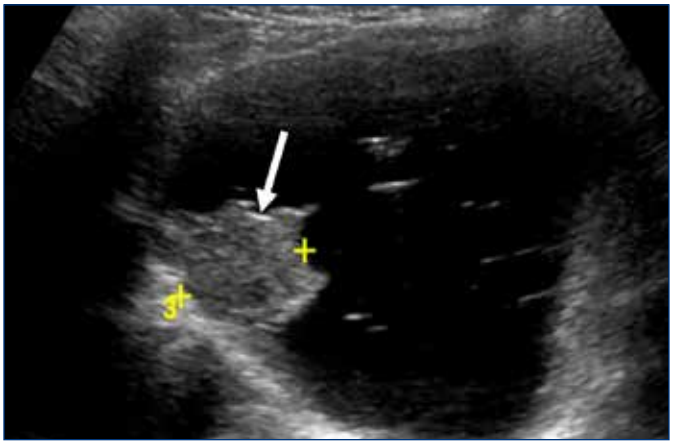
Ultrasonography

Ultrasound can be a useful imaging modality because it is non-invasive, low cost, and it does not expose patients to ionizing radiation. In the United States, the Centers for Medicare & Medicaid Services (CMS) determines the fee for services for patients with Medicare on a national scale; the CMS non-facility price, the rate set for services performed in office, for a bladder ultrasound study is relatively inexpensive at $48.46.[19] However, the role of ultrasound in the evaluation of urothelial carcinoma is currently limited. On initial presentation of a patient with gross hematuria, ultrasound is not a first-line imaging modality due to its relatively low sensitivity. The most recent American College of Radiology (ACR) Appropriateness Criteria places ultrasound in the "May Be Appropriate" category for this use as several studies have shown that ultrasound has relatively poor sensitivity compared to both CT and the gold standard of cystoscopy in the diagnosis of bladder cancer.[20,21] Ultrasound is also in the "May Be Appropriate" category for the initial evaluation of patients with microhematuria with risk factors or without a known benign cause. It is usually not appropriate in patients without known risk factors or with hematuria that is attributable to a non-malignant cause.[20] The ACR has also put out Appropriateness Criteria for the pre-treatment staging of MIBC and the post-treatment surveillance of both NMIBC and MIBC. Ultrasound is deemed to be usually not appropriate for these uses due to its limited ability in visualization beyond the bladder wall which prevents reliable detection of nodal enlargement and identification of MIBC. Whereas for NMIBC, it cannot replace the need for cystoscopic surveillance.[22,23] However, techniques such as 3-D ultrasound rendering and contrast-enhanced sonography have improved the sensitivity of ultrasound to detect bladder cancer at first presentation and discriminate between NMIBC and MIBC, which may lead to increased usage in the future.[24,25]

Optimal ultrasound evaluation of the bladder involves the use of a 3.5–6 MHz transducer to assess the bladder transabdominally in both transverse and longitudinal orientations while the bladder is under moderate distension.[26] Doppler can be useful to identify vascularity within any focal masses present. Spectral Doppler is used to demonstrate arterial or venous blood flow which would be suggestive of bladder cancer (**Figure 1**).[25] Because upwards of 30% of bladder cancers are multifocal, identification of one lesion should lead to the search of other lesions locally.[27]

The most common presentation of visible urothelial carcinoma on ultrasound is a polypoid mass with heterogeneous echotexture arising from the bladder wall, typically located along the posterior wall at the base of the bladder. The mass is immobile, without changes in patient position.[26,27] In MIBC and higher-grade urothelial carcinoma, the mass can invade the musculature and extend into the abdominal wall, prostate, or uterus. Additionally, tumors that arise in bladder

Figure 1. Transverse ultrasound image of a confirmed urothelial carcinoma appearing as a mass arising from the right lateral bladder wall.



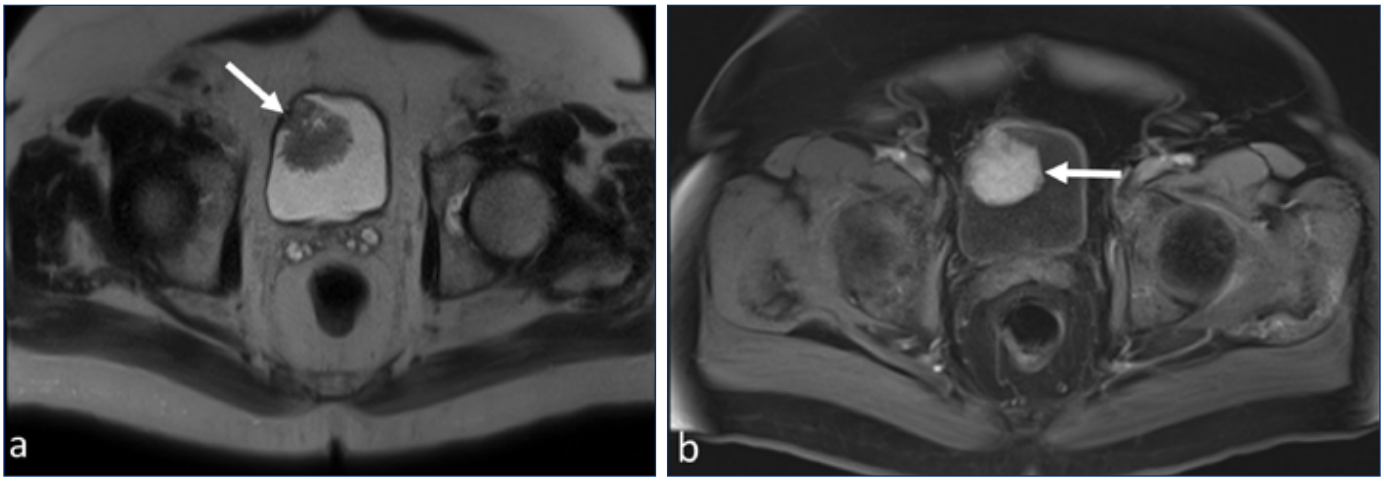
diverticula can have early transmural extension, a sign of poor prognosis.[26] Tumors located at the vesicoureteric junction may cause ureteral obstruction and hydronephrosis, while tumors at the urinary orifice may cause bladder outlet obstruction and urinary retention. In some cases, bladder cancer may appear only as focal wall thickening with or without extension into the lumen. Wall thickening > 3 mm in a well-distended bladder or > 5 mm in a poorly distended bladder is indicative of pathology.[26] Focal calcifications may also be seen in 5% of urothelial carcinomas, with idiopathic focal wall calcifications raising suspicion for an underlying tumor; these can be appreciated on ultrasound as echogenic foci with or without shadowing.[26,27] Important mimics of urothelial carcinoma on ultrasound include other neoplasms such as urachal carcinoma, lymphoma, paraganglioma, metastases, or benign conditions such as cystitis, thrombus, or calculi. Careful sonographic interrogation and thoughtful history or histopathologic correlation are helpful in distinguishing between the aforementioned entities.[26]

MRI

MRI is of increasing interest in bladder cancer due to its high soft-tissue contrast and spatial resolution. MRI is the most expensive imaging modality with a CMS non-facility price totaling $681.73 for assessment of bladder cancer.[19] It is useful for assessing the depth of bladder wall invasion and involvement of adjacent anatomic structures. This makes it a good tool for local staging of bladder cancer. The Vesical Imaging Reporting and Data System (VI-RADS) scoring system was developed in 2018 and has since been consistently validated as a way to standardize the MRI acquisition and interpretation of urothelial cancer using a multiparametric protocol.[28] A 1.5- or 3-T coil should be used and the acquisition protocol should include multiplanar T2-weighted MRI, diffusion-weighted imaging (DWI), and dynamic contrast-enhanced (DCE) MRI to identify tumor extent. Non-fat-saturated T1-weighted sequences are useful for identifying clot or hemorrhage in the bladder and metastases to bone.[28] The field-of-view (FOV) should be large enough to include the entirety of the bladder, proximal urethra, pelvic nodes, prostate, uterus, ovaries, fallopian tubes, and vagina, in accordance with sex.[29] A VI-RADS score is assigned to each of the sequences on a scale from 1 to 5. Scores of 1 and 2 represent tumors unlikely to invade the muscularis propria, while scores of 4 and 5 are likely to invade the detrusor muscle. A score of 3 is equivocal, serving as the cutoff to define MIBC.[30]

A typical suspicious lesion on MRI appears as an intravesical lesion with T2 signal hyperintensity, high DWI signal intensity, low signal intensity at the apparent diffusion coefficient (ADC) map, and early enhancement at DCE-MRI (**Figure 2 a,b**).[28] Furthermore, analyses using ADC values as a biomarker have been demonstrated to correlate with tumor aggressiveness in bladder cancer, with lower ADC values corresponding to more aggressive disease.[28] The layers of the bladder wall that are recognized here from a radiologic perspective are the inner mucosal and submucosal layer, the

Figure 2. MR imaging of muscle invasive urothelial carcinoma. **a**) Axial T2-weighted image showing hypointense anterior mass with detrusor invasion and **b**) axial T1 image demonstrating post-contrast gadolinium enhancement of the mass.



muscularis propria, and the perivesical fat; distinguishing between these layers across different sequences allows for differentiation between NMIBC and MIBC, or higher grade tumors.[28] A tumor may appear as an intramurally growing endophytic mass, an endoluminally growing exophytic mass, a flat lesion, or as a mixed lesion. Of the exophytic masses, these can be sessile or pedunculated papillary masses, and masses with a stalk tend to have more favorable prognoses than those without despite the tumor usually being larger.[28,31] Using DWI, the "inchworm sign" which appears as an archlike shape of high signal intensity with a low signal intensity submucosal stalk, has been proposed to predict aggressiveness. Specifically, its absence can be indicative of lower-stage cancer.[32]

MR urography (MRU) is a special MRI study that is tailored for the evaluation of the urinary system and improves visualization of the upper and lower urinary tracts. MRU makes use of heavily T2-weighted (or static fluid) sequences, utilizing the high signal intensity from urine to image the urinary tract which can be done without contrast enhancement.[33] MRU studies may also include dynamic T1-weighted images acquired after contrast administration to obtain images in three phases. The first is the corticomedullary phase, which is acquired first between 40 and 70 seconds after contrast injection to evaluate the enhanced outer renal cortex and medulla. The next is the nephrographic phase which is acquired 80 to 120 seconds after contrast injection to evaluate the enhanced renal parenchyma. The final phase is the excretory phase, which is acquired 10 to 15 minutes after contrast injection to evaluate the enhanced collecting system.[34] Urothelial tumors may appear as filling defects on the static fluid or excretory phase images, enhance quickly after contrast administration, and tend to have irregular contours at the margins compared to benign entities such as calculi.[34] Comparisons between images obtained immediately after contrast administration and unenhanced T1-weighted images are helpful in detecting enhancement of malignant lesions in the bladder wall.[34]

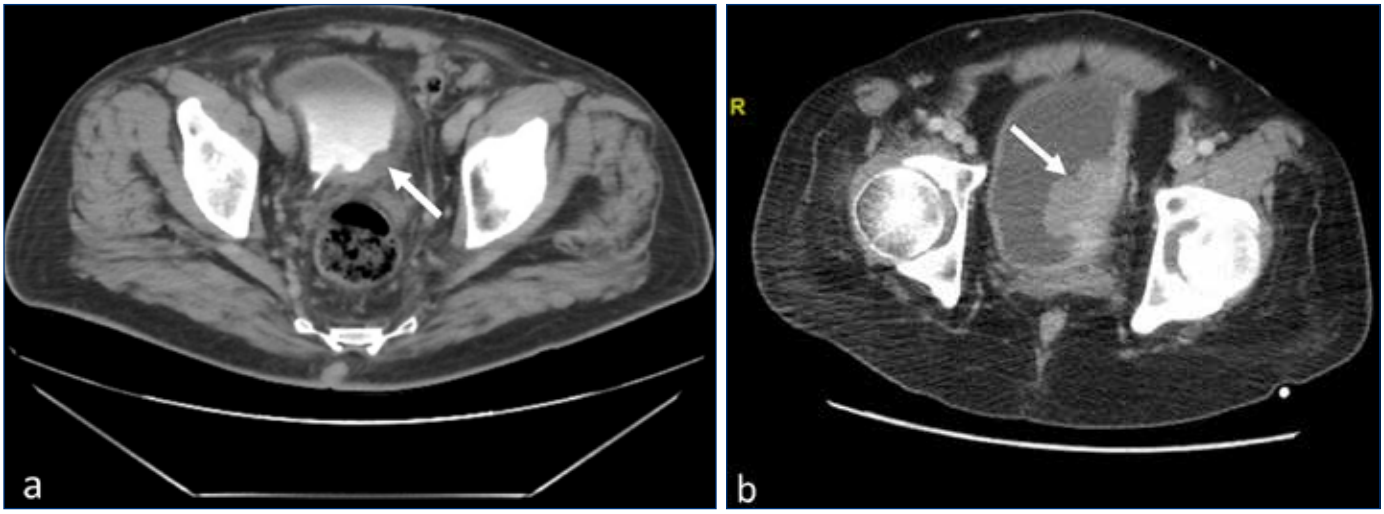
The ACR appropriateness criteria deems MRI abdomen and pelvis (distinguished from MRU) to be usually not appropriate for the evaluation of patients with microhematuria, but notes that MRU may be appropriate for evaluation of pregnant patients or patients with risk factors and no known benign cause of microhematuria.[20] For patients with gross hematuria, MRU is usually appropriate for initial imaging while MRI abdomen pelvis may also be appropriate, noting one study which showed a 98.5% sensitivity in determining the cause of gross hematuria using MRI.[20,35] For locally staging bladder cancer, MRI is noted to be the best imaging modality by the ACR, offering superior soft tissue contrast resolution, sensitivity, and specificity when compared with CT.[22] Additionally, the NCCN guidelines recommend MRI of the abdomen and pelvis if logistically feasible as an option to characterize lesions and evaluate the depth of invasion prior to resection. They recommend MRU as a viable option to evaluate the upper tracts.[18] For post-treatment surveillance, MRU also provides comprehensive evaluation of the genitourinary tract and is usually appropriate to use in NMIBC, and with risk factors or MIBC. MRI abdomen and pelvis without and with IV contrast is usually an appropriate equivalent procedure according to the ACR although there may currently be insufficient evidence for its use in MIBC surveillance compared with MRU. [24]

CT

CT is among the most commonly ordered imaging modalities, and because of its frequent use and impressive spatial resolution, bladder malignancies can often be discovered incidentally on CT. Current NCCN guidelines recommend a CT abdomen and pelvis study prior to transurethral resection if able as an alternative to MRI, and CT urography (CTU) is the preferred study in the evaluation of the upper tract in patients with bladder cancer who can receive IV contrast.[18] The CMS non-facility price of a CTU study is $343.16.[19] CTU differs from a traditional CT pelvis scan in that the protocol includes a precontrast, nephrographic, and excretory phase which is tailored for evaluation of the upper and lower tracts. There are three common protocols used for CTU: the single-bolus technique which involves administering one bolus of contrast with separate arterial, venous, and excretory phase images; the split-bolus technique which involves two administrations of contrast with acquisition in a combined excretory and nephrographic phase; and the triple-bolus technique which involves administration of three small boluses of contrast with acquisition in a combined corticomedullary-nephrographic-excretory phase.[36] The single-bolus technique is the most sensitive for identification of subtle filling defects but the latter techniques reduce the radiation dose significantly.[37]

There are several CT imaging features considered suspicious for malignancy which would warrant further workup with cystoscopy. Focal or multifocal bladder wall thickening in a well-distended bladder is a common imaging finding in urothelial carcinoma, while diffuse wall thickening is rarely representative of malignancy (**Figure 3 a,b**).[37] Although not specific for malignancy, the presence of calcifications in the bladder wall along with wall thickening should also raise concern for malignancy. Discrete bladder nodules or masses, particularly those that are avidly enhancing and are often best appreciated on early phase images, or which result in discrete filling defects in delayed phase images, are also common presentations of malignant lesions.[37] Urothelial carcinomas may also present as abnormal urothelial enhancement with focal areas of hyperenhancement in the absence of a discrete mass, most readily appreciated on early phase images before contrast has been excreted into the bladder.[37] A "stipple sign" has been described on CTU

Figure 3. Contrast-enhanced CT imaging of noninvasive and invasive urothelial carcinoma. **a**) Axial image of noninvasive papillary urothelial carcinoma of the left bladder wall appearing as asymmetric wall thickening. **b**) Axial image of infiltrating high grade papillary urothelial carcinoma in a predominantly left-sided mass.



in urothelial carcinoma with a papillary architecture. It appears as dappled contrast filling in between the papillary projections, though this appearance may sometimes be seen in other entities such as fungus balls and blood clots.[38]

The ACR designates that the standard CT abdomen and pelvis with and without contrast may be appropriate for use in patients with microhematuria and gross hematuria. CTU is usually appropriate for patients with microhematuria with risk factors (and without known benign cause) and for patients with gross hematuria.[20] For pretreatment staging of MIBC, CTU and CT chest abdomen and pelvis with IV contrast are both usually appropriate and complementary.[22] CTU is also usually appropriate in NMIBC with symptoms or risk factors, and MIBC for post-treatment surveillance, with CT abdomen and pelvis with contrast an equivalent alternative for MIBC.[23]

TREATMENT & OUTCOMES

Treatment differs between NMIBC and MIBC, with overall outcomes being much more favorable in NMIBC. In NMIBC, tumors are further stratified into low, intermediate, and high risk based on clinical presentation and presence of risk factors. In low risk NMIBC, transurethral resection of bladder tumor (TURBT) is the first-line treatment with a five-year progression-free survival rate of 93%. With routine cystoscopy surveillance there is no need for upper-tract imaging.[7,18] In intermediate risk NMIBC, TURBT remains the first-line treatment followed by the option of six weeks of induction intravesical therapy, typically with Bacille Calmette-Guérin (BCG) immunotherapy. This results in a five-year progression-free survival rate of 74%, with recommendation for routine cystoscopy and upper tract imaging every one to two years.[7,18] For high risk NMIBC, TURBT with BCG induction and maintenance therapy is the mainstay of treatment, with an option for radical cystectomy if treatment resistant. The five-year progression-free survival rate is 54%, with recommendations for routine cystoscopy and upper tract imaging every one to two years.[7,18]

In MIBC, first-line therapy is neoadjuvant cisplatin chemotherapy followed by radical cystectomy (which confers a survival benefit over bladder sparing options) with a five-year survival rate between 36% and 48%, and recommendations for routine surveillance with CTU or MRU as well as CT or MRI of the chest.[7,18] In metastatic disease, first-line therapy is cisplatin-based chemotherapy or checkpoint inhibitor therapy with agents such as pembrolizumab if ineligible for cisplatin with a five-year survival rate of 5% to 36% depending on how distant the metastases are.[7,18] Recent advances in molecular profiling and pharmacology have led to the approval of targeted therapies by the FDA for some somatic mutations in bladder cancer such as erdafitinib for FGFR-alteration positive cancer with several other clinical trials underway.[40,41]

CONCLUSION

Advances in imaging techniques across multiple modalities in recent years have improved their utility and changed the way that localized and advanced bladder cancer is worked up and managed, though cystoscopy remains the gold standard for characterization today. The therapeutic landscape has also continued to expand, with immunotherapy and targeted therapies seeing more use.

References

1. Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2023. *CA Cancer J Clin*. 2023;73(1):17-48. doi:10.3322/caac.21763
2. Cancer Stat Facts: Bladder Cancer. NIH NCI: Surveillance, Epidemiology, and End Results Program. 2023. Available at: https://seer.cancer.gov/statfacts/html/urinb.html. Accessed October 25, 2023
3. Yu EM, Belay S, Li W, Aragon-Ching JB. Non-urothelial and urothelial variants of bladder cancer. *Cancer Treat Res Commun*. 2022;33:100661. doi:10.1016/j.ctarc.2022.100661
4. Mori K, Abufaraj M, Mostafaei H, et al. A Systematic Review and Meta-Analysis of Variant Histology in Urothelial Carcinoma of the Bladder Treated with Radical Cystectomy. *J Urol*. 2020;204(6):1129-1140. doi:10.1097/JU.0000000000001305
5. Shariat SF, Sfakianos JP, Droller MJ, Karakiewicz PI, Meryn S, Bochner BH. The effect of age and gender on bladder cancer: a critical review of the literature. *BJU Int*. 2010;105(3):300-308. doi:10.1111/j.1464-410X.2009.09076.x
6. Dobruch J, Daneshmand S, Fisch M, et al. Gender and Bladder Cancer: A Collaborative Review of Etiology, Biology, and Outcomes. *Eur Urol*. 2016;69(2):300-310. doi:10.1016/j.eururo.2015.08.037
7. Lenis AT, Lec PM, Chamie K, Mshs MD. Bladder Cancer: A Review. *JAMA*. 2020;324(19):1980-1991. doi:10.1001/jama.2020.17598
8. Uhlig A, Strauss A, Seif Amir Hosseini A, et al. Gender-specific Differences in Recurrence of Non-muscle-invasive Bladder Cancer: A Systematic Review and Meta-analysis. *Eur Urol Focus*. 2018;4(6):924-936. doi:10.1016/j.euf.2017.08.007
9. Lobo N, Afferi L, Moschini M, et al. Epidemiology, Screening, and Prevention of Bladder Cancer. *Eur Urol Oncol*. 2022;5(6):628-639. doi:10.1016/j.euo.2022.10.003
10. van Osch FH, Jochems SH, van Schooten FJ, Bryan RT, Zeegers MP. Quantified relations between exposure to tobacco smoking and bladder cancer risk: a meta-analysis of 89 observational studies. *Int J Epidemiol*. 2016;45(3):857-870. doi:10.1093/ije/dyw044
11. van Osch FHM, Vlaanderen J, Jochems SHJ, et al. Modeling the Complex Exposure History of Smoking in Predicting Bladder Cancer: A Pooled Analysis of 15 Case-Control Studies. *Epidemiology*. 2019;30(3):458-465. doi:10.1097/EDE.0000000000000964
12. Ho CH, Sung KC, Lim SW, et al. Chronic Indwelling Urinary Catheter Increase the Risk of Bladder Cancer, Even in Patients Without Spinal Cord Injury. *Medicine (Baltimore)*. 2015;94(43):e1736. doi:10.1097/MD.0000000000001736
13. Akhtar S, Al-Shammari A, Al-Abkal J. Chronic urinary tract infection and bladder carcinoma risk: a meta-analysis of case-control and cohort studies. *World J Urol*. 2018;36(6):839-848. doi:10.1007/s00345-018-2206-x
14. Xu Y, Huo R, Chen X, Yu X. Diabetes mellitus and the risk of bladder cancer: A PRISMA-compliant meta-analysis of cohort studies. *Medicine (Baltimore)*. 2017;96(46):e8588. doi:10.1097/MD.0000000000008588
15. Ahmadinezhad M, Arshadi M, Hesari E, Sharafoddin M, Azizi H, Khodamoradi F. The relationship between metabolic syndrome and its components with bladder cancer: a systematic review and meta-analysis of cohort studies. *Epidemiol Health*. 2022;44:e2022050. doi:10.4178/epih.e2022050
16. Nassar AH, Abou Alaiwi S, AlDubayan SH, et al. Prevalence of pathogenic germline cancer risk variants in high-risk urothelial carcinoma. *Genet Med*. 2020;22(4):709-718. doi:10.1038/s41436-019-0720-x
17. Edwards TJ, Dickinson AJ, Natale S, Gosling J, McGrath JS. A prospective analysis of the diagnostic yield resulting from the attendance of 4020 patients at a protocol-driven haematuria clinic. *BJU Int*. 2006;97(2):301-305. doi:10.1111/j.1464-410X.2006.05976.x
18. NCCN Guidelines Version 3.2023 Bladder Cancer. Accessed October 25, 2023
19. Medicare Physician Fee Schedule. Centers for Medicare & Medicaid Services. 2024. Available at: https://www.cms.gov/medicare/physician-fee-schedule/search
20. Wolfman DJ, Marko J, Nikolaidis P, et al. ACR Appropriateness Criteria Hematuria. Available at https://acsearch.acr.org/docs/69490/Narrative/. American College of Radiology. Accessed October 25, 2023
21. Tan WS, Sarpong R, Khetrapal P, et al. Can Renal and Bladder Ultrasound Replace Computerized Tomography Urogram in Patients Investigated for Microscopic Hematuria?. *J Urol*. 2018;200(5):973-980. doi:10.1016/j.juro.2018.04.065
22. van der Pol CB, Sahni VA, Eberhardt SC ACR Appropriateness Criteria Pretreatment Staging of Muscle-Invasive Bladder Cancer. Available at https://acsearch.acr.org/docs/69370/Narrative/. American College of Radiology. Accessed October 25, 2023
23. Allen BC, Oto A, Akin O, et al. ACR Appropriateness Criteria Post-treatment Surveillance of Bladder Cancer. Available at https://acsearch.acr.org/docs/69364/Narrative/ . American College of Radiology. Accessed October 25, 2023
24. Ge X, Lan ZK, Chen J, Zhu SY. Effectiveness of contrast-enhanced ultrasound for detecting the staging and grading of bladder cancer: a systematic review and meta-analysis. *Med Ultrason*. 2021;23(1):29-35. doi:10.11152/mu-2730
25. Silva-Ramos M, Louro N, Versos R, Cavadas V, Marcelo F. Does 3D Ultrasound Enhance the Diagnosis of Bladder Tumours in Patients with Haematuria?. *ISRN Urol*. 2012;2012:158437. doi:10.5402/2012/158437
26. Wentland AL, Desser TS, Troxell ML, Kamaya A. Bladder cancer and its mimics: a sonographic pictorial review with CT/MR and histologic correlation. *Abdom Radiol (NY)*. 2019;44(12):3827-3842. doi:10.1007/s00261-019-02276-w
27. Wong-You-Cheong JJ, Woodward PJ, Manning MA, Sesterhenn IA. From the Archives of the AFIP: neoplasms of the urinary bladder: radiologic-pathologic correlation. *Radiographics*. 2006;26(2):553-580. doi:10.1148/rg.262055172
28. Pecoraro M, Takeuchi M, Vargas HA, et al. Overview of VI-RADS in Bladder Cancer. *AJR Am J Roentgenol*. 2020;214(6):1259-1268. doi:10.2214/AJR.20.22763
29. Lawler LP. MR imaging of the bladder. *Radiol Clin North Am*. 2003;41(1):161-177. doi:10.1016/s0033-8389(02)00065-9
30. Panebianco V, Narumi Y, Altun E, et al. Multiparametric Magnetic Resonance Imaging for Bladder Cancer: Development of VI-RADS (Vesical Imaging-Reporting And Data System). *Eur Urol*. 2018;74(3):294-306. doi:10.1016/j.eururo.2018.04.029
31. Wang HJ, Pui MH, Guan J, et al. Comparison of Early Submucosal Enhancement and Tumor Stalk in Staging Bladder Urothelial Carcinoma. *AJR Am J Roentgenol*. 2016;207(4):797-803. doi:10.2214/AJR.16.16283
32. Yajima S, Yoshida S, Takahara T, et al. Usefulness of the inchworm sign on DWI for predicting pT1 bladder cancer progression. *Eur Radiol*. 2019;29(7):3881-3888. doi:10.1007/s00330-019-06119-6
33. Leyendecker JR, Barnes CE, Zagoria RJ. MR urography: techniques and clinical applications. *Radiographics*. 2008;28(1):23-47. doi:10.1148/rg.281075077
34. O'Connor OJ, McLaughlin P, Maher MM. MR Urography. *AJR Am J Roentgenol*. 2010;195(3):W201-W206. doi:10.2214/AJR.09.4176
35. Abou-El-Ghar ME, El-Assmy A, Refaie HF, El-Diasty T. Bladder cancer: diagnosis with diffusion-weighted MR imaging in patients with gross hematuria. *Radiology*. 2009;251(2):415-421. doi:10.1148/radiol.2503080723
36. Raman SP, Horton KM, Fishman EK. Transitional cell carcinoma of the upper urinary tract: optimizing image interpretation with 3D reconstructions. *Abdom Imaging*. 2012;37(6):1129-1140. doi:10.1007/s00261-011-9838-2

37. Raman SP, Fishman EK. Bladder malignancies on CT: the underrated role of CT in diagnosis. *AJR Am J Roentgenol*. 2014;203(2):347-354. doi:10.2214/AJR.13.12021
38. Dyer RB, Chen MY, Zagoria RJ. Classic signs in uroradiology. *Radiographics*. 2004;24 Suppl 1:S247-S280. doi:10.1148/rg.24si045509
39. McLean GK, Pollack HM, Banner MP. The "stipple sign" - urographic harbinger of transitional cell neoplasms. *Urol Radiol*. 1979;1(2):77-79.
40. Dobruch J, Oszczudłowski M. Bladder Cancer: Current Challenges and Future Directions. *Medicina (Kaunas)*. 2021;57(8):749. Published 2021 Jul 24. doi:10.3390/medicina57080749
41. Loriot Y, Necchi A, Park SH, et al. Erdafitinib in Locally Advanced or Metastatic Urothelial Carcinoma. *N Engl J Med*. 2019;381(4):338-348. doi:10.1056/NEJMoa1817323

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Assessing the Trends of Tramadol Utilization in the Medicare Part D Population in Rhode Island

ERIC P. BORRELLI, PhD, PharmD, MBA

ABSTRACT

OBJECTIVE: To assess the trends in tramadol dispensing among Medicare Part D patients in Rhode Island.

METHODS: An analysis was conducted of the Medicare Part D Provider Utilization and Payment Data Public Use File for the years 2013–2021. Chi squared tests were conducted to assess statistical significance of annual changes in proportions.

RESULTS: Following tramadol becoming a controlled substance in 2014, the number of dispensed tramadol prescriptions and patients with a tramadol prescription decreased every subsequent year through 2021 (prescriptions: 42,157 to 33,026; patients: 12,654 to 9,653). The percentage of opioid prescriptions that were tramadol increased from 16.32% in 2013 to 21.19% in 2020.

CONCLUSION: Tramadol utilization has been decreasing among the Medicare Part D population in Rhode Island while the percentage of opioid dispensings that were tramadol have been increasing. Future studies are needed to assess whether patients utilizing tramadol are at a higher risk for adverse outcomes.

KEYWORDS: Tramadol; Utilization; Geriatric; Controlled Substance; Opioids

INTRODUCTION

The opioid epidemic has hit the United States the past couple of decades, with opioid overdose deaths increasing from 21,089 in 2010 to 47,600 in 2017.[1] While fatal opioid overdoses decreased slightly in 2018, they increased to record highs of over 50,000 in 2019, 68,630 in 2020, and 80,411 in 2021.[1] The hardship from the epidemic has especially been true in Rhode Island, which has been hit particularly hard. There have been over 2,500 confirmed accidental overdose deaths in Rhode Island from 2016–2022.[2] Opioids contributed to over 85% of these deaths.[2]

Tramadol is an opioid analgesic that is indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments were inadequate.[3] While it is an opioid agonist, it has a unique mechanism of action which also includes weak inhibition of norepinephrine and serotonin reuptake.[3] In 2014, the United States Drug Enforcement Administration (DEA) classified tramadol as a Schedule IV controlled substance after it was previously a noncontrolled medication.[4]

While tramadol is one of the few opioids that is not a Schedule II controlled substance, that does not necessarily mean that it is a safer opioid.[5-6] Tramadol has nine black boxed warnings listed in its package insert.[3] Additionally, tramadol also had several key drug-drug interactions with central nervous system depressants, cytochrome P450 (CYP) 2D6 inhibitors, CYP 3A4 inhibitors, CYP3A4 inducers, and serotonergic medications as well as drug-disease interactions with patients with a history of epilepsy or seizures, patients with impaired renal function, and patients under the age of 18 following adenoidectomy or tonsillectomy.[3] Additionally, tramadol is included in the American Geriatric Society's Beers Criteria for Potentially Inappropriate Medication Use in Older Adults and is recommended to be used with caution in the geriatric population due to it increasing the risk of hyponatremia or syndrome of inappropriate antidiuretic hormone secretion.[7] Although tramadol has this concerning safety and prescribing profile, it is still a commonly prescribed medication in the United States.

Considering the safety profile of tramadol mixed with the severity of the opioid epidemic, it is important to assess its utilization in real-world settings. Additionally, tramadol's safety profile poses an increased risk of adverse outcome to the geriatric population. Therefore, the objective of this study was to assess the trends in tramadol dispensing among Medicare Part D patients in Rhode Island.

METHODS

An analysis was conducted of the Medicare Part D Provider Utilization and Payment Data Public Use File (PUF) for the years 2013–2021.[8] The PUF database includes all prescription medications billed to Medicare Part D from the outpatient setting on the aggregate drug level. It includes both stand-alone Prescription Drug Plans and Medicare Advantage Prescription Drugs. While this database does include 100% of Medicare Part D patients, it represents approximately only 70% of Medicare patients since about 30% of Medicare patients do not have Part D coverage.[9] More information about this database is available at CMS's website[8] as well as in their methodology documents.[9-11]

The outcomes of interest were the annual number of tramadol prescriptions dispensed, total number of patients with a tramadol prescription dispensed annually, percent of Medicare Part D beneficiaries with a tramadol prescription, annual number of opioid prescriptions, and annual percent of opioid prescriptions that were tramadol. The number of total patients with an opioid prescription was not included. This is due to the fact that the database assessed only provides information on the aggregate drug level without any patient information. While it is possible to calculate the total number of patients with a prescription for each individual opioid, it is possible patients were on more than one opioid within the particular calendar year, and summing all of the patients on each individual opioid would provide an overinflated class estimate. Chi squared tests were conducted to assess statistical significance of annual changes in proportions of Medicare beneficiaries utilizing tramadol as well as annual change in proportion of opioid prescriptions that were tramadol. Chi squared tests were conducted using OpenEpi.[12]

Table 1. Tramadol Utilization among Medicare Part D Beneficiaries in Rhode Island from 2013–2021

Year	Total Tramadol Prescriptions	Total Patients with Tramadol Prescription	Rhode Island Medicare Beneficiaries	Percent of Rhode Island Medicare Patients with a Tramadol Prescription	Percent Change from Prior Year	P value
2021	33,026	9,653	180,885	5.34%	-0.14%	0.0581
2020	34,955	9,657	176,223	5.48%	**-0.37%**	<0.0001
2019	35,368	9,916	169,415	5.85%	**-0.49%**	<0.0001
2018	37,046	10,476	165,199	6.34%	**-0.90%**	<0.0001
2017	39,917	11,578	159,968	7.24%	**-0.84%**	<0.0001
2016	41,792	12,619	156,284	8.07%	**-0.28%**	0.0054
2015	42,157	12,654	151,551	8.35%	**-0.41%**	<0.0001
2014	44,702	12,863	146,834	8.76%	0.12%	0.2692
2013	42,514	12,271	141,959	8.64%		

Table 2. Prescription Opioid Utilization among Medicare Part D Beneficiaries in Rhode Island from 2013–2021

Year	Total Tramadol Prescriptions	Total Non-Tramadol Opioid Prescriptions	Total Opioids Opioid Prescriptions	Percent of Opioids Prescriptions that were Tramadol	Percent Change from Prior Year	P value
2021	33,026	131,098	164,124	20.12%	**-1.07%**	<0.0001
2020	34,955	130,009	164,964	21.19%	**0.62%**	<0.0001
2019	35,368	136,547	171,915	20.57%	**0.55%**	<0.0001
2018	37,046	147,932	184,978	20.03%	**0.68%**	<0.0001
2017	39,917	166,395	206,312	19.35%	**0.71%**	<0.0001
2016	41,792	182,388	224,180	18.64%	**0.62%**	<0.0001
2015	42,157	191,803	233,960	18.02%	0.06%	0.5803
2014	44,702	204,227	248,929	17.96%	**1.64%**	<0.0001
2013	42,514	218,009	260,523	16.32%		

RESULTS

In Rhode Island, the number of tramadol prescriptions dispensed annually increased from 42,514 in 2013 to 44,702 in 2014 for Medicare Part D patients (**Table 1**). Following 2014, the number of dispensed tramadol prescriptions decreased every subsequent year from 42,157 in 2015 to 33,026 in 2021. Following the same trend, the number of patients with a tramadol prescription increased from 12,271 in 2013 to 12,863 in 2014. Following 2014, the number of patients with a dispensed tramadol prescription decreased every subsequent year from 12,654 in 2015 to 9,653 in 2021. These decreases happened while the number of Medicare Part D beneficiaries in Rhode Island increased every year from 141,959 in 2013 to 180,885 in 2021.

When assessing the percentage of Medicare beneficiaries with a tramadol dispensing, there was a non-significant increase from 2013 to 2014 (8.76% vs 8.64%, p=0.2692). After 2014, there was a significant decrease annually with 8.35% of Medicare beneficiaries in 2015 to 5.48% in 2020. 2021 also saw a decrease in the percentage of Medicare beneficiaries with a tramadol prescription; however, this decrease was not statistically significant (5.34%, p=0.0581).

The number of non-tramadol opioids dispensed decreased every year from 218,009 in 2013 to 130,009 in 2020, with 2021 seeing a slight increase with 131,098 (**Table 2**). When assessing all opioid prescriptions, the percentage that were tramadol increased every year from 16.32% in 2013 to 21.19% in 2020 (all annual increases were statistically significant except from 17.96% in 2014 to 18.02% in 2015 p=0.5803). The percent of opioids that were tramadol then saw a significant decrease from 21.19% in 2020 to 20.12% in 2021 (p<0.0001).

DISCUSSION

This analysis found that among the Medicare Part D population in Rhode Island, tramadol's utilization (both in number of prescriptions and number of beneficiaries with a prescription) increased from 2013 to 2014, before decreasing in the years following it becoming classified as a Schedule IV controlled substance through 2021. While tramadol's utilization decreased following 2014, the percentage of opioid prescriptions dispensed to the Medicare Part D population in Rhode Island that were tramadol increased every year through 2020 before slightly decreasing in 2021.

In August 2014, the DEA classified tramadol as a Schedule IV controlled substance after being noncontrolled.[4] This occurred within months of hydrocodone being reclassified as a Schedule-II controlled substance from being a Schedule III.[13] While tramadol went from being noncontrolled to being a controlled substance, several studies found that its utilization actually increased in the years following it being a controlled substance.[14-18] Several theories as to why this occurred exist. One is that while tramadol became a controlled substance, it had a lower abuse classification compared to the other opioid medications and is therefore a "safer" opioid.[5,6] Additionally, with hydrocodone becoming a Schedule-II controlled substance, more restrictions were placed on its prescribing such as limiting to maximum 30-day supplies, not allowing refills, and before electronic prescriptions became more readily available, patients had to physically pick up a hard copy prescription from their prescriber and bring it to their pharmacy. Even though tramadol had more restrictions than it did before (maximum five refills), it still could be written with refills and up to 90-day supplies, and have prescriptions called or faxed into the pharmacy. While several studies saw these trends, it was not found in this study of Medicare Part D patients in Rhode Island which found a nonsignificant increase in percentage of Medicare Part D beneficiaries utilizing tramadol from 2013–2014 followed by a statistically significant decrease every subsequent year through 2020. However, the percentage of prescription opioids that were tramadol increased annually, indicating that of the opioids being prescribed, tramadol's use was increasing versus its comparators. The existence and increased utilization of state Prescription Drug Monitoring Programs (PDMPs) has helped assist prescribers and pharmacists in the process of prescribing and dispensing controlled substances, like tramadol, in Rhode Island.[19-22] The Rhode Island PDMP allows prescribers and dispensing pharmacists the opportunity to see all controlled substances a patient is getting, regardless of prescriber or pharmacy, allowing an assessment of potentially concurrent utilization in instances of drug-drug interactions with controlled substances.[22,23]

Tramadol is one of the few non-Schedule II opioids, indicating it has a lower abuse potential compared to other agents in its class. However, several studies have come out in the past decade detailing tramadol having a higher risk of chronic opioid utilization compared to other opioid options.[24-27] Most of these studies assessed initial opioid therapy for opioid naive patients, with consistent results found both in the commercially insured population as well as the Medicare population. While it was outside the scope of this study to assess and outside the capabilities of the database of this analysis, future studies are needed to assess whether patients initiating opioid therapy on tramadol have a higher risk of chronic opioid utilization compared to other short-acting opioid medications.

The findings that the number of Medicare Part D patients with a tramadol prescription as well as total annual number of tramadol prescriptions decreasing annually from 2014 in Rhode Island is similar to findings on the state level for all patients in Rhode Island. An analysis of the Rhode Island PDMP was conducted of the years 2017-2021 assessing the dispensings of opioids, benzodiazepines, and stimulants among Rhode Island residents.[28] They found that for all residents in Rhode Island, the number of tramadol prescriptions decreased annually from 90,361 in 2017 to 67,593 in 2021.[28] However, contrary to our findings in the Medicare population specifically, the percentage of opioid prescriptions that were tramadol did not vary much during this time period, ranging from a low of 15.7% in 2017 to a high of 16.6% in 2020.[28] Additionally, while the number of patients with a tramadol prescription increased from 39,145 to 41,626 from 2017 to 2018, the number of patients decreased the following three years from 38,501 in 2019 to 35,303 in 2021.[28]

Another finding from this analysis shows that while tramadol utilization, both number of patients and number of prescriptions, has been decreasing annually since 2014 when tramadol became a controlled substance, the percentage of opioids that were tramadol prescriptions has been increasing annually with the exception of 2021. The implications of these findings are difficult to decipher without having further clinical information, which is not provided in this database. Without having clinical diagnoses, it is impossible to know whether tramadol was a more appropriate therapy option than other opioid therapies (i.e., treating diabetic peripheral neuropathy)[29] or less appropriate option (patients with seizure disorders).[3]

Additionally, without having additional clinical information in the database such as medication utilization by patient, it is not possible to know if tramadol was being prescribed safely. Tramadol has a host of drug-drug interactions that increase the risk of adverse outcomes for patients when taken concurrently. These drug-drug interactions include interactions with central nervous system depressants, CYP 2D6 inhibitors, CYP 3A4 inhibitors, CYP3A4 inducers, and serotonergic medications.[3] Additionally, tramadol has been shown to increase the risk of QT prolongation or torsade de pointes, with the risk being heightened among patients with concurrent utilization of other QT prolonging medications.[3]

A study assessing tramadol utilization in a large population of commercially insured and Medicare Advantage patients found that almost one in three patients with a tramadol prescription had a clinically significant concurrent drug-drug or drug-disease interaction.[30] They also found that compared to commercially insured patients, Medicare patients 65 years and older had significantly higher odds of concurrent tramadol utilization with every interacting drug class assessed except for nonbenzodiazepine sedative hypnotics as well as for every drug-disease interaction after adjusting for clinical and demographic covariables.[30] Medicare patients younger than 65 years had significantly higher adjusted odds of tramadol utilization for every drug-drug and drug-disease category assessed than both commercially insured patients as well as Medicare patients 65 years and older.[30] They also found that generalists compared to other specialties were more likely to prescribe to patients with concurrent utilization of interacting medications but less likely among patients with drug-disease and condition interactions.[30] Several analyses of emergency department prescribing in the United States found tramadol prescribing increasing annually with a dramatic increase following it becoming a controlled substance in 2014 through 2017 and 2018.[16,18] While the trends of tramadol utilization are decreasing in Rhode Island in the Medicare Part D population, it would be important to assess whether patients utilizing tramadol are under higher risk of adverse outcomes due to drug-drug or drug-disease interactions.

Several studies have shown adverse outcomes of patients utilizing tramadol. A propensity-score matched cohort study conducted in Spain found that compared to codeine, new utilizers of tramadol had significantly higher risk of all-cause mortality (hazard ratio (HR): 2.31, 95% CI: 2.08–2.56), cardiovascular events (HR: 1.15, 95% CI: 1.05–1.27), and fractures (HR: 1.50, 95% CI: 1.37–1.65).[31] A propensity-score matched cohort study in the United Kingdom of individuals at least 50 years of age with osteoarthritis found that patients utilizing tramadol had significantly higher rates of all-cause mortality compared to patients utilizing naproxen (HR: 1.71, 95% CI: 1.41–2.07), diclofenac (HR: 1.88, 95% CI: 1.51–2.35), celecoxib (HR: 1.70, 95% CI: 1.33–2.17), and etoricoxib (HR: 2.04, 95% CI: 1.37–3.03) while having no significant difference compared to codeine (HR: 0.94, 95% CI: 0.83–1.05).[32] Similar findings were observed in an propensity-score matched cohort study in Canada which found tramadol having a significantly higher risk of all-cause mortality compared to naproxen (HR: 1.2, 95% CI: 1.0–1.4), diclofenac (HR: 1.3, 95% CI: 1.1–1.5), Cox-2 inhibitors (HR: 1.5, 95% CI: 1.3–1.8), but no significant difference compared to codeine (HR: 0.9, 95% CI: 0.7–1.1).[33] In addition to its potential increased risk in all-cause mortality, a systematic literature review of case studies and case series conducted in 2020 found 127 cases of unintentional overdose deaths involving tramadol.[34] While 70% involved concomitant utilization of central nervous system depressants, there were eight reports of tramadol utilization being the sole cause of death.[34]

Several limitations exist in addition to what has already been stated. One limitation is that while this analysis does include every Medicare Part D patient who had a prescription dispensed that was billed to Medicare, it does not include all Medicare patients as only 70% of Medicare patients have prescription coverage through Medicare Part D.[9] Additionally, this only includes prescriptions that were billed to Medicare, and does not include prescriptions that were paid for out of pocket (either because insurance did not cover the prescription and the patient still proceeded to fill the medication, or if the patient opted not to have the prescription filled through their insurance), workers compensation, or other means. Additionally, it only represents prescriptions filled in the outpatient pharmacy setting, and not prescriptions that were dispensed in inpatient settings.

CONCLUSION

Trends in tramadol utilization have been decreasing among the Medicare Part D population in Rhode Island following tramadol's classification as a controlled substance. While tramadol's utilization has been decreasing, the percentage of opioids that were tramadol have been increasing. Considering tramadol's concerning safety profile, future studies are needed to assess whether patients utilizing tramadol are at a higher risk for adverse outcomes.

References

1. National Institute on Drug Abuse. Drug Overdose Death Rates. National Institute on Drug Abuse. 2023 Jun 30. Available at: https://nida.nih.gov/research-topics/trends-statistics/overdose-death-rates. Accessed January 21, 2024.
2. Weidele HR, Omari J, Rodriguez M, Hallowell BD. Accidental Drug Overdose Deaths in Rhode Island: January 1, 2016-December 31, 2022. R I Med J (2013). 2023 Sep 1;106(8):42-44.
3. Tramadol [package insert]. Coral Springs, FL; ACI Healthcare USA, Inc.; 2023.
4. United States Federal Register. Schedules of Controlled Substances: Placement of Tramadol Into Schedule IV. United States Federal Register. 2014 Jul 2;79(127):37623-37630. Available at: https://www.govinfo.gov/content/pkg/FR-2014-07-02/pdf/2014-15548.pdf. Accessed February 4, 2024.
5. Stannard C. Tramadol is not opioid-lite'. BMJ. 2019 May 14;365.
6. Miotto K, Cho AK, Khalil MA, Blanco K, Sasaki JD, Rawson R. Trends in Tramadol: Pharmacology, Metabolism, and Misuse. Anesth Analg. 2017 Jan;124(1):44-51.
7. The 2023 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2023 Jul;71(7):2052-2081.
8. Centers for Medicare and Medicaid Services. Medicare Part D Prescribers - by Provider and Drug. Centers for Medicare and Medicaid Services. Available at: https://data.cms.gov/provider-summary-by-type-of-service/medicare-part-d-prescribers/medicare-part-d-prescribers-by-provider-and-drug. Accessed December 21, 2024.

9. Centers for Medicare and Medicaid Services. Medicare Fee-For Service Provider Utilization & Payment Data Part D Prescriber Public Use File: A Methodological Overview. Centers for Medicare and Medicaid Services. November 6, 2020. Available at: https://www.cms.gov/research-statistics-data-and-systems/statistics-trends-and-reports/medicare-provider-charge-data/downloads/prescriber_methods.pdf. Accessed January 23, 2024.
10. Centers for Medicare and Medicaid Services. Medicare Part D Prescribers Datasets: Technical Specifications. Centers for Medicare and Medicaid Services. August 2021. Available at: https://data.cms.gov/sites/default/files/2021-08/mup_dpr_ry21_20210819_technical_specifications.pdf. Accessed January 23, 2024.
11. Centers for Medicare and Medicaid Services. Medicare Part D Prescribers - by Provider and Drug Data Dictionary. Centers for Medicare and Medicaid Services. Available at: https://data.cms.gov/sites/default/files/2022-07/MUP_DPR_RY22_20220715_DD_PRV_Drug.pdf. Accessed January 23, 2024.
12. Dean AG, Sullivan KM, Soe MM. OpenEpi: Open Source Epidemiologic Statistics for Public Health, Version. www.OpenEpi.com, updated 2013/04/06, accessed 2024/01/14.
13. United States Federal Register. Schedules of Controlled Substances: Rescheduling of Hydrocodone Combination Products From Schedule III to Schedule II. United States Federal Register. 2014 Aug 22. 79 (163): 49661-49682. Available at: https://www.govinfo.gov/content/pkg/FR-2014-08-22/pdf/2014-19922.pdf. February 4, 2024.
14. Gupta S, Nguyen TD, Freeman PR, et al.: Competitive Effects of Federal and State Opioid Restrictions: Evidence from the Controlled Substance Laws. Cambridge, MA: National Bureau of Economic Research, 2020. Available at https://www.nber.org/papers/w27520. Accessed February 10, 2024.
15. Bigal LM, Bibeau K, Dunbar S: Tramadol prescription over a 4-year period in the USA. Curr Pain Headache Rep. 2019; 23 (10):76.
16. Rui P, Santo L, Ashman JJ. Trends in opioids prescribed at discharge from emergency departments among adults: United States, 2006-2017. Natl Health Stat Report. 2020;135:1-12.
17. Seago S, Hayek A, Pruszynski J, Newman MG. Change in prescription habits after federal rescheduling of hydrocodone combination products. Proc (Bayl Univ Med Cent). 2016 Jul;29(3):268-70.
18. Mullins PM, Mazer-Amirshahi M, Pourmand A, Perrone J, Nelson LS, Pines JM. Tramadol Use in United States Emergency Departments 2007-2018. J Emerg Med. 2022 May;62(5):668-674.
19. Green TC, Mann MR, Bowman SE, Zaller N, Soto X, Gadea J, Cordy C, Kelly P, Friedmann PD. How does use of a prescription monitoring program change medical practice? Pain Med. 2012 Oct;13(10):1314-23.
20. Green TC, Mann MR, Bowman SE, Zaller N, Soto X, Gadea J, Cordy C, Kelly P, Friedmann PD. How does use of a prescription monitoring program change pharmacy practice? J Am Pharm Assoc (2003). 2013 May-Jun;53(3):273-81.
21. Cordy C, Kelly P. Patterns of prescribing – the Rhode Island prescription monitoring program. R I Med J (2013). 2013 Nov 1;96(11):36-7.
22. McDonald JV. Using the Rhode Island Prescription Drug Monitoring Program (PMP). R I Med J (2013). 2014 Jun 2;97(6):64-5.
23. Rhode Island Department of Health. Prescription Drug Monitoring Program. Rhode Island Department of Health. 2024. Available at: https://health.ri.gov/healthcare/medicine/about/prescriptiondrugmonitoringprogram/. Accessed February 28, 2024.
24. Musich S, Wang SS, Slindee L, Kraemer S, Yeh CS. Characteristics associated with transition from opioid initiation to chronic opioid use among opioid-naïve older adults. Geriatr Nurs. 2019 Mar-Apr;40(2):190-196.
25. Kern DM, Zhou S, Chavoshi S, Tunceli O, Sostek M, Singer J, LoCasale RJ. Treatment patterns, healthcare utilization, and costs of chronic opioid treatment for non-cancer pain in the United States. Am J Manag Care. 2015 Mar 1;21(3):e222-34.
26. Shah A, Hayes CJ, Martin BC. Characteristics of Initial Prescription Episodes and Likelihood of Long-Term Opioid Use - United States, 2006-2015. MMWR Morb Mortal Wkly Rep. 2017 Mar 17;66(10):265-269.
27. Wackerbarth JJ, Ham SA, Aizen J, Richgels J, Faris SF. Persistent Opioid Usage After Urologic Intervention and the Impact of Tramadol. Urology. 2021 Nov;157:114-119.
28. Paiva TJ, Nitenson AZ, Antinozzi D, Onyejekwe C, McDonald JV, Hallowell BD. Dispensed Opioid, Buprenorphine, Benzodiazepine, and Stimulant Prescriptions among Rhode Island Residents, 2017-2021. R I Med J (2013). 2023 Mar 1;106(2):27-30.
29. Price R, Smith D, Franklin G, Gronseth G, Pignone M, David WS, Armon C, Perkins BA, Bril V, Rae-Grant A, Halperin J, Licking N, O'Brien MD, Wessels SR, MacGregor LC, Fink K, Harkless LB, Colbert L, Callaghan BC. Oral and Topical Treatment of Painful Diabetic Polyneuropathy: Practice Guideline Update Summary: Report of the AAN Guideline Subcommittee. Neurology. 2022 Jan 4;98(1):31-43.
30. Borrelli EP, Bratberg J, Greaney ML, Kogut SJ. Tramadol utilization among patients with higher risk of adverse drug events: A claims analysis of commercially insured and Medicare Advantage members. J Opioid Manag. 2023 May-Jun;19(3):257-271.
31. Xie J, Strauss VY, Martinez-Laguna D, Carbonell-Abella C, Diez-Perez A, Nogues X, Collins GS, Khalid S, Delmestri A, Turkiewicz A, Englund M, Tadrous M, Reyes C, Prieto-Alhambra D. Association of Tramadol vs Codeine Prescription Dispensation With Mortality and Other Adverse Clinical Outcomes. JAMA. 2021 Oct 19;326(15):1504-1515.
32. Zeng C, Dubreuil M, LaRochelle MR, Lu N, Wei J, Choi HK, Lei G, Zhang Y. Association of Tramadol With All-Cause Mortality Among Patients With Osteoarthritis. JAMA. 2019 Mar 12;321(10):969-982.
33. Li L, Marozoff S, Lu N, Xie H, Kopec JA, Cibere J, Esdaile JM, Aviña-Zubieta JA. Association of tramadol with all-cause mortality, cardiovascular diseases, venous thromboembolism, and hip fractures among patients with osteoarthritis: a population-based study. Arthritis Res Ther. 2022 Apr 11;24(1):85.
34. Alrashdi S, Paudyal V, Elnaem MH, Cheema E. Causes, nature and toxicology of tramadol-associated deaths reported in the peer-reviewed literature: a systematic review of case studies and case series. Drugs &Therapy Perspectives. 2021 Sep;37(9): 422-32.

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Taking the Pulse of the Nursing Home Industry in Rhode Island

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ABSTRACT

INTRODUCTION: Nursing home facilities in Rhode Island face unprecedented challenges today. Most facilities find themselves in a difficult financial position with thin – or negative – operating margins. In addition, Rhode Island enacted new minimum staffing regulations for nursing homes in 2021. Facilities that fail to meet the new staffing requirements would incur significant financial penalties. The persistent shortage of direct care staff, however, limits administrators' ability to hire the workers needed to meet the required staffing levels.

METHODS: We conducted an online survey of nursing home administrators at all of the licensed nursing facilities in Rhode Island over 30 days from September to October 2023. We received responses from 53 out of 77 nursing home administrators, for an overall response rate of 69%.

RESULTS: A majority of respondents reported numerous vacancies for clinical staff at their facilities. Most administrators felt that it was difficult to hire new staff, despite a variety of financial incentives to recruit workers. As a result, nursing homes were unable to comply with Rhode Island's new minimum staffing requirements.

CONCLUSION: Nursing homes in Rhode Island continue to experience a chronic staffing shortage. Furthermore, since a majority of nursing homes in Rhode Island have a negative operating margin, enforcing the state's minimum staffing requirements would impose significant financial hardship on the state's nursing facilities.

KEYWORDS: nursing homes, staffing requirements, nursing shortage, certified nurse assistants, financial performance

INTRODUCTION

Nursing homes in Rhode Island face unprecedented staffing challenges. Turnover among registered nurses (RNs), licensed practical nurses (LPNs), and certified nurse assistants (CNAs) increased in recent years, leading to chronic staffing shortages. In 2021, the passage of the Nursing Home Staffing and Quality Care Act established the nation's strictest minimum staffing requirements for nursing homes. Under § 23-17.5-32 of the RI General Laws, nursing homes must provide residents with an average of 3.58 hours of direct care per resident day (HPRD) beginning on January 1, 2022, and 3.81 HPRD beginning on January 1, 2023.[1] The new law, however, created a Catch-22 for nursing facilities. While failure to meet the new staffing requirements would result in significant financial penalties, the ongoing shortage of nurses and certified nurse assistants (CNAs) left nursing homes unable to hire the staff needed to meet the new required ratios. Nursing homes argued that they could not comply with the new law because of ongoing staffing constraints.[2]

Soon after the law was scheduled to take effect in 2022, Rhode Island Governor Dan McKee issued an executive order that suspended its enforcement. The Rhode Island Department of Health continued its administrative rulemaking process, issuing final regulations to implement the law in December 2022.[3] To date, the Department of Health has not imposed any fines on facilities that failed to meet the new requirements. However, the looming threat of significant financial penalties became a major topic of conversation during the 2022 and 2023 legislative sessions.[2] In December 2023, McKee declared that a state of emergency existed in the state's nursing home industry and suspended the monetary penalties for nursing homes that failed to meet the state's minimum staffing requirements under §23-17.5-33 of the RI General Laws.[4] In his latest executive order, the governor noted that "Rhode Island nursing homes have lost over 2,000 employees since December of 2019, and Rhode Island nursing homes have lost 20% of their workforce since 2020."[4] The "estimated net costs of enforcing the minimum staffing levels… would be approximately $60 million, further straining nursing home resources and potentially resulting in additional closures and forcing the relocation of residents."[4]

In addition, nursing homes also face the prospect of new federal staffing requirements. On September 1, 2023, the Centers for Medicare & Medicaid Services (CMS) proposed to establish minimum staffing requirements for the nation's 15,000+ nursing homes. Under the proposed rule, Medicare and Medicaid-certified long-term care facilities must provide 0.55 hours per resident day (HPRD) for registered nurses (RNs) and 2.45 HPRD for certified nursing assistants

(CNAs). All facilities must also ensure that an RN is always onsite.[5] A recent study prepared by Abt Associates for the Centers for Medicare and Medicaid Services, however, found that "no single staffing level that would guarantee quality care," undercutting the Biden administration's regulatory initiative just days before it was announced.[6]

A recent survey by the American Health Care Association – an industry trade association – found that 54% of facilities operated at a loss in 2023 and an additional 34% had a total margin between 0–3%.[7] Furthermore, 45% of facilities surveyed reported that they "can't sustain operations at the current pace for more than one year."[7] The potential of nursing home closures, consolidations, or limits on admissions due to staffing constraints threatens access to care for vulnerable patients. To gauge the potential impact of new staffing requirements on nursing homes in Rhode Island, we surveyed all nursing home administrators in the state to gather information about their financial position, current staffing levels, and strategies to recruit and retain clinical staff. In addition, we also inquired about how regulations under consideration in other states (such as California's recent decision to raise the minimum wage for healthcare workers to $25/hour) would impact their facilities.

METHODS

Our survey explored the ability of nursing home facilities to comply with new regulations in the context of the current healthcare job market. Our survey instrument was modeled after a semi-annual survey of nursing home administrators conducted by the American Health Care Association.[7] We assembled a list of all 77 nursing home administrators in the state with the assistance of the state's two long-term care associations – the Rhode Island Health Care Association (RIHCA) and Leading Age RI. Based on feedback from Leading Age RI and the Rhode Island Health Care Association, we adjusted our instrument to better differentiate staffing levels for CNAs, LPNs, and RNs. We also modified the AHCA survey's questions to incorporate more detail about facilities' financial position. We incorporated new questions to gauge the impact of Rhode Island's staffing regulations, the adequacy of Medicaid reimbursement, and recent proposals to raise the minimum wage for healthcare workers and penalize facilities with lower occupancy rates. We do not report data on individual facilities or institutions. No identifying information about patients or staff was collected. Our survey methodology and questionnaire were reviewed by the Providence College Institutional Review Board and found exempt from IRB review.

The survey was administered electronically; administrators received an email that included a link to an anonymous web survey form. Each email invitation also included a consent form for participants. Responses were collected over one month, from September 5 to October 5, 2023. In addition to sending out weekly reminders to our email distribution list, the executive directors of both the RIHCA and LeadingAge RI also encouraged their member facilities to complete the survey. Our survey had an overall response rate of 69%. This is a much higher response rate than is typically obtained in online surveys, where the average response rate is 44%.[13] Participating facilities are located in each of the state's five counties, including 30 in Providence, six each in Bristol and Washington, and five each in Kent and Newport. Most (N=45) participants worked at for-profit nursing homes, while eight represented non-profit institutions. For-profit nursing homes had a higher response rate (70%) than non-profit providers (57%).

RESULTS

Most nursing homes in Rhode Island experienced staffing shortages in 2023 (**Table 1**). Since January 2023, facilities reported that their staffing situation had improved more for CNAs and LPNs than for RNs (**Table 2**). A majority of facilities reported that it was either 'very difficult' or 'somewhat difficult' to hire new nursing staff (**Table 3**).

Table 1. Current Levels of Nurse Staffing by Position Type

Staffing level	CNAs No. (%)	LPNs No. (%)	RNs No. (%)
Fully staffed	1 (2)	15 (28)	3 (6)
Some unfilled positions	21 (40)	26 (49)	29 (55)
Many unfilled positions	28 (53)	8 (15)	14 (26)
Severely understaffed	3 (6)	3 (6)	7 (13)
Preferred not to answer	0 (0)	1 (2)	0 (0)

Table 2. Change in Nurse Staffing Since January 2023 by Position Type

Staffing situation	CNAs No. (%)	LPNs No. (%)	RNs No. (%)
Much worse	2 (4)	3 (6)	5 (9)
Somewhat worse	12 (23)	11 (21)	17 (32)
Stayed the same	17 (32)	24 (45)	23 (43)
Somewhat better	15 (28)	12 (23)	8 (15)
Much better	7 (13)	2 (4)	0 (0)
Prefer not to answer	0 (0)	1 (2)	0 (0)

Table 3. Difficulty of Hiring New Staff by Position Type

Level of Difficulty	CNAs No. (%)	LPNs No. (%)	RNs No. (%)
Very difficult	19 (36)	9 (17)	32 (62)
Somewhat difficult	29 (55)	32 (60)	18 (35)
Somewhat easy	5 (9)	9 (17)	2 (4)
Very easy	0 (0)	2 (4)	0 (0)
Prefer not to answer	0 (0)	1 (2)	0 (0)

Administrators cited a variety of factors that influenced staff turnover at their facilities. The most frequent sources of employee turnover included understaffing (17/53; 32%) and dissatisfaction with salary/wages (15/53; 28%). Nursing homes employed several strategies to recruit and retain workers in the context of the state's tight healthcare labor market. Over the past six months, facilities used financial incentives such as increasing wages (49/53; 92%), signing bonuses for new staff (42/53; 79%), additional benefits (24/53; 45%), and providing retention bonuses for existing staff (20/53; 38%). In addition, most facilities also sought to strengthen their workplace culture (42/53; 79%) and invested more in staff training and education (36/53; 68%). Our survey revealed that most providers struggle to hire workers in the current job market; administrators cited a lack of interested candidates (45/53; 85%) and the inability to meet applicants' salary demands (41/53; 77%) as the principal obstacles they faced in hiring new employees.

In response to ongoing staffing shortages, nearly all (51/53; 96%) of facilities asked current staff to work overtime or extra shifts in recent months. Most facilities (37/53; 70%) also reported hiring temporary agency staff to fill staffing shortfalls. More than a third of nursing homes (20/53; 38%) limited new admissions or closed a unit, wing, or floor (11/53; 21%) in recent months due to staffing shortages.

Nearly two-thirds (34/53; 64%) of Rhode Island nursing homes reported a negative total operating margin (calculated by dividing operating profit by its total revenue and expressing it as a percentage) and almost half of respondents (25/53; 47%) reported a negative total margin of greater than 5%. In contrast, only three facilities (6%) reported a positive operating margin. This question had the highest non-response rate in our survey, with nearly one-third of participating facilities (16/53; 30%) electing not to answer.

Most (35/53; 66%) nursing homes reported that they would be unable to meet the new staffing levels established by the 2021 Nursing Home Staffing and Quality Care Act; only 12 facilities (23%) reported that they could comply with the minimum staffing requirements. Furthermore, administrators indicated that the implementation of the state's new staffing requirements would have a significant impact on their facilities' financial position (**Table 4**). A majority of administrators were either 'very concerned' (11/53; 21%) or 'somewhat concerned' (18/53; 35%) that they might have to close their facilities as a result of ongoing workforce shortages.

Our survey also explored the impact of potential policy changes on nursing homes in Rhode Island. California's SB 525, for example, raised the minimum wage for healthcare workers to $25 per hour.[8] Industry groups estimated that the implementation of a similar requirement in Connecticut could cost facilities $700 million annually.[9] Legislators in Connecticut also recently considered a bill that would impose financial penalties on facilities that have occupancy rates below 90% over a twelve-month period.[10] Both policies would have a significant impact on nursing homes in Rhode Island that could lead to facility closures, mergers, limits on new admissions, operating deficits, and the closure of units, wings, or floors (**Table 5**).

Table 4. Impact of Enforcing Rhode Island's New Minimum Staffing Requirements

Response	No. (%)
No impact	0 (0)
My facility would limit admissions	4(8)
My facility would close units, wings, or floors	3 (6)
My facility would increase the use of temporary staff	7 (13)
My facility would run an operating deficit	14 (27)
My facility would explore a merger/acquisition	5 (10)
My facility would close	13 (25)
Prefer not to answer	6 (11)

Table 5. Impact of Potential Policy Changes on Nursing Homes

Response	Financial Penalties for Facilities with Occupancy Rates Below 90%	Raising the Minimum Wage to $25/hour
No impact	4 (7.5)	0 (0)
My facility would limit admissions	9 (17)	8 (15)
My facility would close units, wings, or floors	12 (23)	9 (17)
My facility would increase the use of temporary staff	11 (21)	8 (15)
My facility would run an operating deficit	23 (43)	26 (49)
My facility would explore a merger/acquisition	11 (21)	14 (26)
My facility would close	19 (36)	21 (40)
Other	4 (7.5)	3 (6)
Prefer not to answer	10 (19)	9 (17)

Limitations

Since our survey only includes responses from 53 of the state's 77 licensed nursing home facilities, our results may not reflect the views of all nursing home administrators. Non-participating facilities may differ in significant ways from those who responded to the survey. In addition, our survey presents a snapshot of the nursing home industry in Rhode Island at a point of time in the Fall of 2023. Changing labor market conditions and public policies could affect administrators' views since we administered our survey.

CONCLUSION

Policymaking does not occur in a vacuum. Our study demonstrates that efforts to improve nursing home staffing must consider the economic impact of the new regulations on providers. Understaffed nursing homes struggle to recruit direct care workers in a competitive labor market where hospitals and other providers often offer higher wages and better working conditions. The AHCA's mid-year survey of nursing homes in 2023 found that a 'lack of interested or qualified candidates' was a significant obstacle to hiring.[7] While hiring new staff appears to be a greater concern for Rhode Island's nursing homes in the current environment without new initiatives to retain workers, the ongoing staffing challenges facing long-term care providers are likely to remain. As noted above, only 38% of nursing home facilities in Rhode Island offered longevity or retention bonuses to existing employees – in contrast to the 79% of facilities that provided bonuses for new hires.

Rhode Island's experience is not unique. Neighboring states are struggling with similar challenges that led policymakers to delay the implementation of higher staffing requirements for nursing home facilities.[11] As the president of the Connecticut Health Care Association noted, "The supply of workers for hire is simply insufficient in this environment. Compliance with a higher standard would not be achievable due to the shortage of workers."[11] In October 2023, the Connecticut Association of Health Care Facilities sued the state to block the implementation of higher staffing ratios for nursing homes, "arguing that state officials went beyond the intent of the legislature in enacting specific requirements."[12] In New York, the Department of Health issued notices of noncompliance to nursing homes in August 2023; facilities that do not meet the state's 2022 staffing mandate can be fined $2,000 per day. The fines, however, remain 'in limbo' since the New York Department of Health acknowledged that a shortage of healthcare workers hinders compliance with the law, which could allow nursing homes to appeal any penalties.[12] Furthermore, it remains unclear what staffing level would lead to significant improvements in patient care outcomes.[6]

Both the Biden administration's proposed staffing mandate and the staffing requirements established by Rhode Island's 2021 nursing home reform legislation have far-reaching impacts on the nursing home industry. Our study found that most nursing homes are unable to comply with Rhode Island's new staffing requirements. Furthermore, most facilities are currently operating in the red. Without additional funding, hiring more workers to comply with the new staffing requirements will further weaken the financial position of the state's nursing homes. Since most nursing home patients are covered by Medicaid, most facilities are price-takers, not price-setters. Low Medicaid reimbursement limits the ability of nursing homes to offer more competitive wages and benefits. A recent study of nursing homes in Pennsylvania, for example, found that "low Medicaid reimbursement rates are a key contributor to quality shortfalls in this industry."[14] Following a 10% increase in Medicaid spending, nursing homes increased the number of skilled nurses by 8.7%.[14] Higher Medicaid reimbursement rates, in short, are an essential element of a long-term strategy to address the ongoing staffing shortage in Rhode Island nursing facilities.

John Gage, the president of the Rhode Island Health Care Association, noted that if Governor McKee had not suspended the enforcement of the staffing mandate, "fines of more than $65 million resulting from the staffing mandate would have been issued to seventy-three (73) Rhode Island nursing facilities for the period of July 1, 2022 through September 30, 2023."[15] Since several facilities have recently closed in Rhode Island or now operate under court-ordered receivership, any effort to penalize nursing home facilities for failure to meet the state's staffing mandates is likely to diminish access to care for patients and place more facilities at risk of closure. Nursing home closures, in turn, could have significant side effects for hospitals in Rhode Island. If nursing homes close or are forced to limit admissions because of an inability to meet higher staffing requirements, patient discharges to post-acute care settings could be impacted. In Massachusetts, for example, hundreds of patients remained hospitalized awaiting discharge to skilled nursing facilities in November 2023 because of a shortage of available beds.[16]

Until the labor market for CNAs, LPNs, and RNs improves, imposing fines on facilities that cannot hire enough staff will only exacerbate the financial challenges facing long-term care providers in Rhode Island. Before requiring nursing homes to hire additional staff to meet higher staffing ratios, policymakers must first explore options to train more clinical staff in a competitive job market.[17] Training and recruiting new direct care staff, however, will do little to address the ongoing shortage unless facilities have more resources to offer higher wages and improved working conditions to their employees.

References

1. State of Rhode Island, General Laws § 23-17.5-32. https://webserver.rilegislature.gov//Statutes/TITLE23/23-17.5/23-17.5-32.htm.
2. Gregg K. RI never enforced nursing home minimum staffing requirements. Why the law might change. *Providence Journal*. 2023, May 31. https://www.providencejournal.com/story/news/politics/2023/05/31/ris-highest-in-the-nation-nursing-home-staffing-law-entwined-in-end-of-session-talks/70273928007/.
3. Center for Health Facilities Regulation, Rhode Island Department of Health. Nursing Home Minimum Staffing Levels Enforcement Manual and Procedures. 2022, December. https://health.ri.gov/publications/policies/nursing-home-minimum-staffing-level-enforcement.pdf.
4. McKee, DJ. Amended Order Preserving the Availability of Resident Care in State Nursing Facilities. Executive Order 22-18. February 14, 2022. https://governor.ri.gov/executive-orders/executive-order-22-18.

5. Center for Medicare and Medicaid Services (CMS). Medicare and Medicaid Programs: Minimum Staffing Standards for Long-Term Care Facilities and Medicaid Institutional Payment Transparency Reporting (CMS 3442-P). September 1, 2023. https://www.cms.gov/newsroom/fact-sheets/medicare-and-medicaid-programs-minimum-staffing-standards-long-term-care-facilities-and-medicaid.
6. Rau J. CMS study sabotages efforts to boost nursing home staffing, advocates say. *Kaiser Health News*. 2023, August 29. https://kffhealthnews.org/news/article/cms-study-nursing-home-staffing-levels/.
7. American Health Care Association. State of the Nursing Home Industry: Mid-Year 2023. 2023; June 6. https://www.ahcancal.org/News-and-Communications/Fact-Sheets/FactSheets/SNF%20Survey%20Mid-Year%202023.pdf.
8. Prager D, Levandowski A. California creates first minimum wage requirement for healthcare workers. Nixon Peabody. 2023, October 30. https://www.nixonpeabody.com/insights/alerts/2023/10/30/california-creates-first-minimum-wage-requirement-for-healthcare-workers.
9. Towhey J. LTC wage hike effort headed for run-in with state minimum staffing proposal. *McKnight's Long Term Care News*. 2023, February 15. https://www.mcknights.com/news/ltc-wage-hike-effort-headed-for-run-in-with-state-minimum-staffing-proposal/.
10. Altimari D, Martinez JL. CT nursing homes that don't fill 90% of beds could be fined under new proposal. *CT Mirror*. 2023, March 1. https://www.ctinsider.com/politics/article/nursing-homes-ct-beds-17812046.php.
11. Towhey J. With legislators unable to stomach cost, proposed staffing rule likely to die. *McKnight's Long Term Care News* 2023, May 10. https://www.mcknights.com/news/with-legislators-unable-to-stomach-cost-proposed-staffing-rule-likely-to-die/
12. Henrekson J. Fines suspended for nursing homes that violate minimum staffing law. McKnight's Long-Term Care News. 2024, January 3. https://www.mcknights.com/news/fines-suspended-for-nursing-homes-that-violate-minimum-staffing-law/.
13. Wu MJ, Zhao K, Fils-Aime F. Response rates of online surveys in published research: A meta-analysis. *Computers in Human Behavior Reports*. 2022;7. https://doi.org/10.1016/j.chbr.2022.100206.
14. Hackman MB. Incentivizing Better Quality of Care: The Role of Medicaid and Competition in the Nursing Home Industry. *Am Econ Rev* 2019 May;109(5):1684–1716. doi: 10.1257/aer.20151057.
15. Farzan A. RI mandated the highest nursing home staffing in the US. Why the governor suspended penalties. *Providence Journal* 2023; December 29. https://www.providencejournal.com/story/news/politics/2023/12/29/fines-suspended-indefinitely-for-rhode-island-nursing-homes-that-violate-minimum-staffing-law/72061342007/.
16. Massachusetts Health and Hospital Association. Throughput Survey Report: Number of Patients Awaiting Discharge to Post-Acute Settings. 2023; November. https://mhalink.informz.net/mhalink/data/images/November%202023%20Throughput%20Survey%20Report.pdf.
17. Hackey RB. RI Leaders need to invest in the long-term care workforce. *Providence Business News*. 2023; February 3. https://pbn.com/r-i-leaders-need-to-invest-in-long-term-care-workforce/.

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Cholangiocarcinoma: Epidemiology and Imaging-Based Review

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ABSTRACT

Cholangiocarcinoma (CCA) is a rare cancer of the bile duct epithelium, and in the last few decades its incidence rate has been increasing. It is associated with a high mortality rate due to late diagnosis and its aggressive nature. Many risk factors have been identified; some are more common in certain regions than others. CCA can be classified according to its anatomical location or macroscopic growth pattern, the latter being most helpful for imaging interpretation. Clinical features can vary from obstructive-like symptoms to nonspecific symptoms, such as weight loss and malaise. Imaging, specifically MRI/MRCP, is crucial in diagnosing CCA, staging, and treatment planning. Surgery with chemotherapy is the mainstay treatment option, and other palliative treatment options exist for those who have unresectable disease.

KEYWORDS: Cholangiocarcinoma, Imaging, MRI, MRCP, CT, Ultrasound, Biliary Tract

INTRODUCTION

Cholangiocarcinoma (CCA) is the second most common form of primary liver neoplasm but makes up less than 2% of all cancers.[1,2] CCAs represent a diverse set of aggressive malignancies arising from different locations of the biliary tract, excluding those deriving from the gallbladder or ampulla of Vater. The development of CCA is poorly understood, but a complex interaction between genetics and multiple risk factors is suggested.

Trending the incidence rate of CCA has proved difficult due to misclassification of CCAs and changes in the International Classification of Diseases for Oncology (ICD-O) coding over time. However, in the past few decades a global rise in CCA incidence has been observed.[3] Geographically, incidence is highest in Eastern Asia countries such as Thailand, where age-adjusted incidence rates are as high as 85 per 100,000 compared to the reported rate of between 0.8 to 2 per 100,000 in the Western world.[3,4]

Diagnosis of CCA depends on clinical suspicion, laboratory tests, and imaging, with surgical resection being the gold standard for treatment. Despite medical advances over the past few decades, prognosis remains poor due to late presentation, high rate of recurrence, and aggressive nature of the tumor. Some studies have reported a five-year survival rate as low as 5%, and up to 75% of patients die within the first year of diagnosis.[5] This review provides a brief overview of CCA, diagnostic steps, treatment options, and associated outcomes.

CHOLANGIOCARCINOMA

CCAs are categorized into three main types based on anatomical location: intrahepatic, extrahepatic, and perihilar. Perihilar CCA is the most prevalent, making up 50–60% of CCA cases, followed by distal CCA (20–30%) and intrahepatic CCA (10–20%).[1,6] CCA can also be classified based on macroscopic growth patterns: mass-forming, intraductal growing, and periductal infiltrating. Mass-forming CCAs are solid intrahepatic tumors discrete from the surrounding liver parenchyma, and they tend to metastasize within the liver. Intraductal growth is mainly confined to the biliary tract lumen and is the least aggressive subtype. The periductal subtype usually involves surrounding portal structures and grows longitudinally, and it can invade neighboring liver parenchyma; however, it is not associated with a solid mass like mass-forming CCAs and has a predilection to metastasize to hilar lymph nodes.[7,8,9] Morphologic descriptions can aid with imaging interpretation and diagnosis.

Intrahepatic cholangiocarcinoma (iCCA) can arise from large intrahepatic ducts peripheral to the left and right hepatic ducts or smaller ducts located within the periphery of the liver parenchyma.[7,10] Morphologically, the mass-forming type makes up about 60%, while intraductal and periductal types comprise 20% of all iCCAs.[11] iCCAs can be fibrotic, an important feature that gives it a characteristic imaging appearance, and in 20% of cases, can cause capsular retraction.[12]

Extrahepatic cholangiocarcinoma (eCCA), an umbrella term for perihilar cholangiocarcinoma (pCCA), also known as Klatskin tumor, and distal cholangiocarcinoma (dCCA), makes up 70–80% of CCA cases. Anatomically, pCCA is located central to the left and right hepatic ducts but peripheral to the cystic duct. These tumors are classified according to the degree of biliary tract involvement (Bismuth-Corlette classification) and can be labeled as Type 1, Type 2, Type 3A/3B, and Type 4. Meanwhile, dCCA is central to the cystic duct and involves the common bile duct.[13]

EPIDEMIOLOGY

CCA usually presents between the fifth and seventh decade of life, with men being more affected than women. Patients with increased risk factors, those with primary sclerosing cholangitis (PSC) or congenital abnormality of the biliary tree, can present decades earlier compared to those with average risk.[14] CCA is uncommon in the Western world, with incidence rates less than 2 per 100,000, but incidence can increase by 40-fold in endemic areas, such as Thailand.[4] Recently, increasing incidence rates have been reported globally.[3] In the United States, a sharp rise in iCCA compared to eCCA has also been noted, with a 350% increase in iCCA incidence rate compared to a 20% increase with eCCA. This rise in CCA incidence rate has been observed across different races, sexes, and ethnicities.[13,15] Another study looking at a 40-year trend in the incidence of CCA in the United States reports an increase in iCCAs from .44 to 1.18 per 100,000. In contrast, the incidence of eCCAs has been stable from 1973 to 2012.[16] Hispanic patients have a higher incidence rate, 1.22 per 100,000, while African Americans have the lowest incidence rate at 0.3 per 100,000. Specifically, in Rhode Island, incidence rates have also increased in the past decades (**Table 1**).

Risk factors vary based on geographical location. For example, parasites are considered a significant risk factor for developing CCA in East Asian countries, where infections with the liver fluke *Opisthorchis viverrini*, are common. Primary sclerosing cholangitis (PSC) and fibropolycystic liver disease are considered important risk factors for developing CCA in Western countries.[17] Almost 50% of patients develop CCA within one year of PSC diagnosis.[18] Thorotrast, a now-banned contrast agent, is also strongly associated with CCA. The literature describes many important risk factors involving the pathogenesis of CCAs. These risk factors, however, only account for a minority of CCA cases and vary in global distribution.[1,19,20]

CLINICAL FEATURES

The clinical presentation of patients with CCA can differ depending on the subtype of CCA. Patients with eCCA typically present with obstructive symptoms, such as jaundice, due to the anatomical location of eCCA. Most patients with iCCA are asymptomatic or have nonspecific signs, with about 12-30% of cases being found incidentally at an advanced stage of disease.[21] Initial workup includes obtaining a right upper quadrant ultrasound and blood test for bilirubin levels, serum aminotransferases (ALT), alkaline phosphatase (ALP), and gamma-glutamyltransferase (GGT) levels. Additional serological tests, including CA 19-9 and CEA, can also aid in diagnosing CCA. CA 19-9 and CEA levels require careful interpretation as both can be elevated in many benign conditions.[22] Alpha-fetoprotein (AFP), specific for hepatocellular carcinoma (HCC), can help distinguish between iCCA and HCC since both present as solid liver tumors and share similar risk factors.[23]

IMAGING FEATURES

The diagnostic approach in symptomatic patients depends on suspicion of CCA, patient history of PSC, and suspected CCA type. Patients with obstructive symptoms or right upper quadrant pain usually undergo transabdominal ultrasound since it can quickly confirm dilatation and obstruction and help rule out benign causes such as gallstones.[24] If suspicion for CCA remains high, additional imaging with cross-sectional imaging can be considered. Cross-sectional imaging is crucial for diagnosing CCA, as it assists in characterizing tumors, detecting metastases, and assessing vasculature involvement. These aspects are integral for staging and treating CCA effectively. It is also crucial to consider other diseases, specifically HCC and metastases to the liver.

Transabdominal Ultrasound

Transabdominal ultrasound (TAUS) has a high sensitivity for identifying and localizing the site of obstruction. A study with 429 patients examining the diagnostic accuracy of TAUS found it to have 89% and 94% sensitivity for identifying and localizing the site of obstruction, respectively.[25] Imaging findings can vary depending on the type of CCA. iCCA tends to present as a large mass with ill-defined and irregular borders, with varying echogenicity (**Figure 1**). Depending on the tumor's location, eCCA may only cause intrahepatic dilation or dilation of both intrahepatic and extrahepatic ducts. Dilation of the biliary duct greater than 6 mm, in the absence of gallstones, is considered to be due to obstructive lesions in an average-risk patient.[25] Patients with PSC may not show bile duct dilatation on TAUS, but worsening of duct dilation and the presence of dominant stricture makes CCA highly likely.[26] The differential for a hepatic mass includes HCC and liver metastases. On ultrasound, the presence of solid nodule(s) exhibiting diverse

Table 1. Demographics and age-adjusted incidence rate of cholangiocarcinoma (ICD-O-3 8160/3) in RI (1995–2019)

Demographics	Mean Age (years)	Male (%)	White(%)		
	67.89 ± 12.73	50.66	89.6		
Incidence	1995–1999	2000–2004	2005–2009	2010–2014	2015–2019
Age-adjusted incidence rate, per 100,000 individuals	1.10	0.85	1.27	1.84	2.18

Figure 1. Transverse ultrasound images of the right hepatic lobe demonstrate a solid irregular hypoechoic mass (white arrow), measuring 3.71 x 3.42 x 3.23 cm.

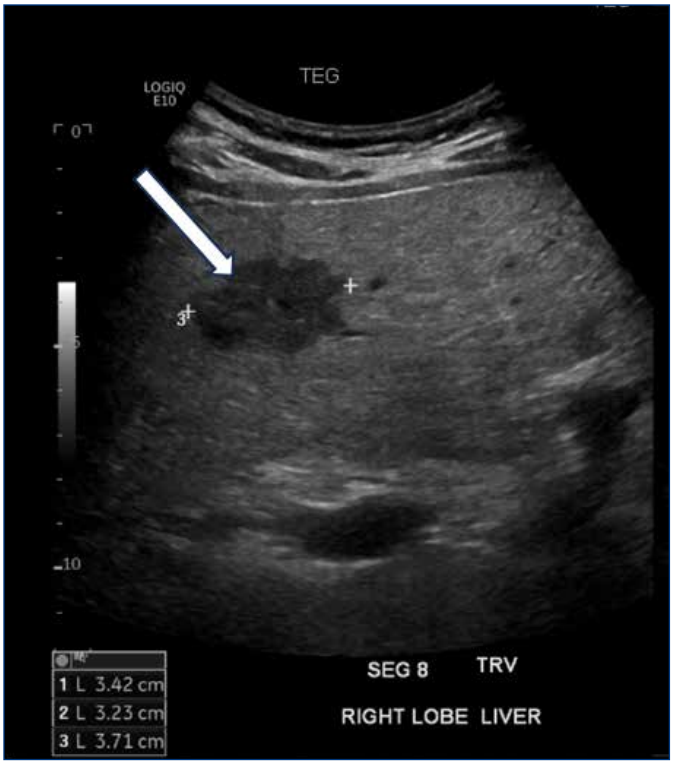
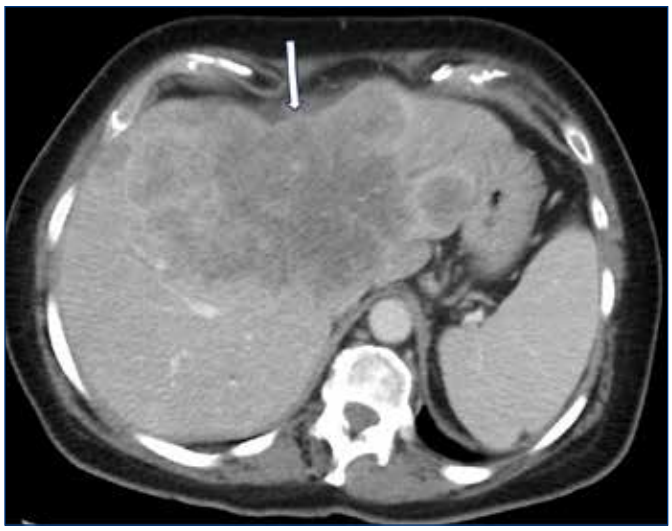


Figure 2. Axial CT image demonstrates numerous hypodense masses in the liver, with a dominant mass with indistinct margins centered in hepatic segment 4. Capsular retraction can also be seen adjacent to the mass (white arrow)



echogenicity and homogeneity, along with irregular borders, is indicative of HCC. HCC on contrast-enhanced ultrasound (CEUS) can present with enhancement in the arterial phase due to neovascularity and it's followed by a washout phase during the portal venous phase.[27] Liver metastases have a diverse presentation and ultrasound is rarely used given its limitations.[28]

Computed Tomography

If suspicion for CCA is high, computed tomography (CT) can be considered for initial imaging. It can accurately identify intrahepatic masses and locate obstructions. In its portal venous phase, it can differentiate between benign and malignant causes of intrahepatic strictures.[12,29] iCCAs can present as large non-capsulated hypodense masses with peripheral duct dilation and peripheral enhancement (arterial and venous phases) with late centripetal spread. These hypodense lesions can either be poorly or well-differentiated and can display liver capsular retraction depending on its stromal component (**Figure 2**).[12,30] The rare mixed hepatocellular-cholangiocellular carcinoma (HCC-CCA), a subtype of iCCA, may show imaging patterns distinct from that of HCC and CCA and often requires biopsy for confirmation.[31]

Contrast is necessary for working up CCA, as its different phases can reveal additional information necessary for diagnosis, staging and treatment planning. The arterial phase can reveal important vascular anatomy of the liver and surrounding structures, which is crucial for surgical planning. In the portal venous phase, iCCA shows weak peripheral contrast enhancement with low intratumoral attenuation. The size of the tumor and the presence of satellite nodules can be deduced. In late-phase scan, usually 10 minutes after contrast injection, a peripheral washout with a centripetal spread can be seen. Sometimes, this delayed enhancement may not appear. Taken together, the late-phase scan can give a sneak peek into the makeup of the tumor. Tumors with high fibrosis display late centripetal contrast due to contrast trapping, and tumors with necrosis and/or mucin fail to enhance.[32]

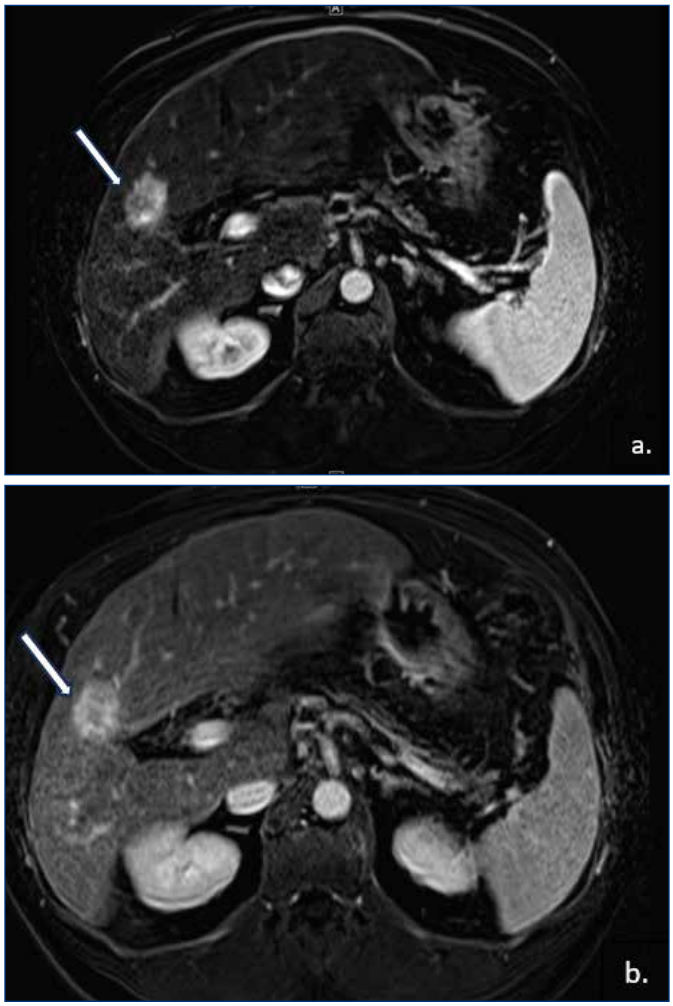
With eCCAs, lesions can be localized based on where ductal dilation is observed. pCCA lesions arise near the perihilar region, and imaging features depend on the degree of bile duct involvement. Bilateral intrahepatic duct dilatation or non-union of the left and right hepatic duct, without gallbladder distension, is suggestive of pCCA. Tumors arising from either left or right hepatic duct can be large, with intrahepatic duct dilation proximal to the tumor and with liver parenchyma infiltration. Dilation of both intrahepatic and extrahepatic ducts with gallbladder distension indicates a centrally located lesion suggestive of dCCA.[1,33] When compared with its main differential consideration, HCC on CT presents as a hypodense or isodense lesion with non-rim arterial phase hyperenhancement followed by rapid washout in the portal venous phase.[34] The other more common differential consideration, liver metastases, tend to be hypovasular and present as a hypodense lesion during the portal venous phase, where the liver parenchyma enhances.[28]

Magnetic Resonance Imaging

Due to its superior soft tissue contrast and ability to provide detailed anatomical information about the biliary tract, magnetic resonance imaging (MRI), in conjunction with magnetic resonance cholangiopancreatography (MRCP), is currently the modality of choice for diagnosing and staging CCA.[35] MRI is crucial for preoperative planning as it can accurately evaluate the extent of the tumor, vascular involvement, and resectability, thus having a significant impact on surgical outcomes.[36] In patients with PSC, MRI/MRCP is utilized for surveillance since the lifetime incidence of CCA is higher than non-PSC patients. In recent years, MRCP has become the imaging of choice over traditional invasive procedures, like endoscopic retrograde cholangiopancreatography (ERCP), for examining the biliary tract. MRCP is purely diagnostic compared to ERCP, which can also be used for therapeutic purposes; however, this is a small trade-off as MRCP has been found to be more effective at identifying obstructive lesions and analyzing the extent of the lesion compared to ERCP.[37]

One study comparing MRI/MRCP to CT with direct cholangiography on the ability to evaluate tumor extent and resectability of bile duct cancer found that MRI/MRCP has a similar diagnostic capability to that of CT, with a diagnostic rate of 90.7% and 87% for lesions involving the secondary biliary confluences and intrapancreatic common bile duct, respectively. CT showed a similar diagnostic rate at 85.1% and 87%, and the difference in the performance between the two was not statistically significant ($p>0.05$).[38] On MRI, mass-forming iCCAs can present as hypointense lesions on T1-weighted imaging or heterogeneously hyperintense with central hypointensity on T2-weighted imaging. Similar to CT, MRI can show initial peripheral enhancement with gradual centripetal spread after contrast injection. Delayed central enhancement, combined with peripheral washout, can give the lesions a targetoid appearance (**Figure 3**).[39] Periductal growth presents with wall thickening at the level of the lesion with peripheral ductal dilation and late-phase contrast enhancement. On contrast-enhanced MRI, mixed HCC-CCA can display irregular shape with sharp rim enhancement in the early dynamic phases without targetoid appearance. This targetoid appearance favors CCA and can help to differentiate it from HCC.[40] Specifically, HCC on MRI presents as a hypointense mass on T1-weighted sequences and a hyperintense mass on T2-weighted sequences, with marked arterial hyperenhancement on the arterial phase followed by portal venous phase washout.[34] Alternatively, metastatic lesions presentation can vary based on the primary cancer, but usually present as hypointense lesions on T1-weighted sequences and hyperintense lesions on T2-weighted sequences, with enhancement. Metastatic lesions do not retain contrast during the hepatobiliary phase when hepatocyte-specific MRI contrast agents such as eovist are used.[28]

Figure 3. [**a**] Axial T1 post-contrast subtraction non-delayed and [**b**] three-minute delayed with the targetoid appearance. MR images demonstrate avid enhancement of the right hepatic lesion (white arrows).

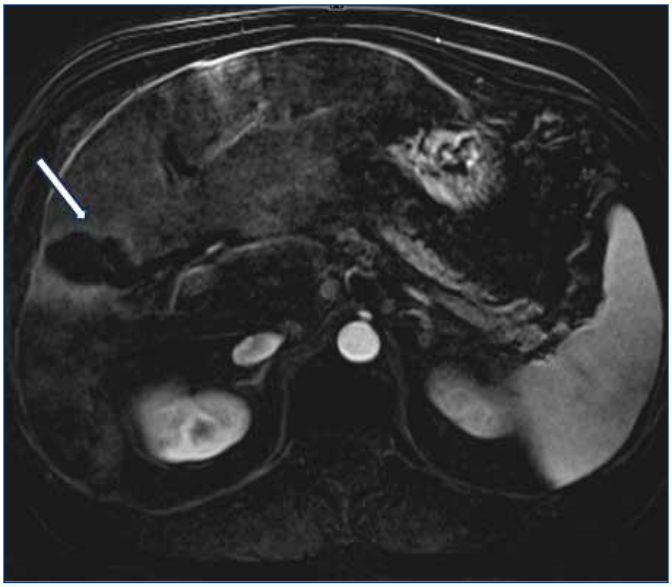


TREATMENT AND OUTCOMES

Surgical resection with curative intent is the mainstay treatment for CCA. However, only 25% of patients have resectable CCA.[41] The National Comprehensive Cancer Network (NCCN) recommends six months adjuvant therapy with capecitabine in patients who underwent surgical resection with negative margins and negative regional nodes.[42] The phase III trial of the BILCAP study demonstrated a significant improvement in overall survival for patients who received eight cycles of capecitabine compared to the control group.[43] The NCCN recommends either durvalumab or pembrolizumab in combination with gemcitabine and cisplatin for patients with unresectable or metastatic disease, as indicated by findings from the phase III TOPAZ-1 and phase III randomized KEYNOTE-966 trials.[42,44,45]

Other treatment options, such as liver transplantation or locoregional therapies can be considered. Liver transplantation, previously contraindicated in pCCA, is another option

Figure 4. Axial T1 post-contrast subtraction MR image demonstrating no enhancement associated with right hepatic lesion (white arrow), one month post-ablation.



for treating CCA. A single-center retrospective study of 216 patients with early-stage unresectable pCCA who received liver transplantation following neoadjuvant chemoradiotherapy demonstrated a five-year disease-free survival of 65% and with an intent-to-treat five-year survival of 53%.[46] Some evidence exists for the use of locoregional therapies, such as radiofrequency ablation, transarterial chemoembolization, and transarterial radioembolization, but these treatment options mainly serve palliative purposes (**Figure 4**).[47,48] Recommendations for use also vary depending on the expert groups.

CONCLUSION

Cholangiocarcinoma (CCA) is a rare and aggressive liver cancer associated with poor outcomes. Over the past couple of decades, the incidence rate of CCA has been rising globally. Specifically, in the United States, this increase in incidence has been observed across different races, sexes, and ethnicities. Because incidence rate and risk factors vary significantly around the world, with rates highest in Southeast Asia, the complex roles of environment, genetics, and socioeconomic status in the pathogenesis of CCA are difficult to elucidate. Regardless, it is challenging to diagnose CCA due to its indolent course. Patients in whom CCA is suspected should undergo appropriate imaging, namely MRI with MRCP or CT, for tumor characterization and staging. Although surgery with curative intent is the gold standard for treating CCA, the prognosis remains poor due to late presentation and high recurrence rate. Adjuvant chemotherapy is recommended post-resection, and for unresectable cases, systemic therapy and other palliative treatment may be considered. Ultimately, CCA is challenging to detect and even more challenging to treat. Given its rising incidence globally, further study of CCA's risk factors, means to achieve earlier diagnosis, and more effective surgical and medical treatment options is paramount.

References

1. Shin DW, Moon S-H, Kim JH. Diagnosis of Cholangiocarcinoma. *Diagnostics*. 2023; 13(2):233. https://doi.org/10.3390/diagnostics13020233
2. Vanderveen KA, Hussain HK. Magnetic Resonance Imaging of cholangiocarcinoma. *Cancer Imaging*. 2004;4(2):104-115. Published 2004 Apr 6. doi:10.1102/1470-7330.2004.0018
3. Florio AA, Ferlay J, Znaor A, Ruggieri D, Alvarez CS, Laversanne M, Bray F, McGlynn KA, Petrick JL. Global trends in intrahepatic and extrahepatic cholangiocarcinoma incidence from 1993 to 2012. Cancer. 2020;126:2666–2678.
4. Daines WP, Rajagopalan V, Grossbard ML, Kozuch P. Gallbladder and biliary tract carcinoma: A comprehensive update, Part 2. *Oncology (Williston Park)*. 2004;18(8):1049-1068.
5. Mosconi S, Beretta GD, Labianca R, Zampino MG, Gatta G, Heinemann V. Cholangiocarcinoma. Crit Rev Oncol Hematol. 2009;69:259–270.
6. Sarcognato S, Sacchi D, Fassan M, et al. Cholangiocarcinoma. *Pathologica*. 2021;113(3):158-169. doi:10.32074/1591-951X-252
7. Sasaki A, Aramaki M, Kawano K, et al. Intrahepatic peripheral cholangiocarcinoma: mode of spread and choice of surgical treatment. *Br J Surg*. 1998;85(9):1206-1209. doi:10.1046/j.1365-2168.1998.00815.x
8. Shimada K, Sano T, Sakamoto Y, Esaki M, Kosuge T, Ojima H. Surgical outcomes of the mass-forming plus periductal infiltrating types of intrahepatic cholangiocarcinoma: a comparative study with the typical mass-forming type of intrahepatic cholangiocarcinoma. *World J Surg*. 2007;31(10):2016-2022. doi:10.1007/s00268-007-9194-0
9. Suh KS, Roh HR, Koh YT, Lee KU, Park YH, Kim SW. Clinicopathologic features of the intraductal growth type of peripheral cholangiocarcinoma. *Hepatology*. 2000;31(1):12-17. doi:10.1002/hep.510310104
10. Yamasaki S. Intrahepatic cholangiocarcinoma: macroscopic type and stage classification. *J Hepatobiliary Pancreat Surg*. 2003;10(4):288-291. doi:10.1007/s00534-002-0732-8
11. Oseini AM, Chaiteerakij R, Shire AM, Ghazale A, Kaiya J, MoserCD, Aderca I, Mettler TA, Therneau TM, Zhang L, et al. Utility of serum immunoglobulin G4 in distinguishing immunoglobulin G4-associated cholangitis from cholangiocarcinoma. Hepatology. 2011;54:940–948.
12. Valls C, Gumà A, Puig I, Sanchez A, Andía E, Serrano T, Figueras, J. Intrahepatic peripheral cholangiocarcinoma: CT evaluation. Abdom. Imaging 2000, 25, 490–496.
13. Banales JM, Marin JJG, Lamarca A, et al. Cholangiocarcinoma 2020: the next horizon in mechanisms and management. *Nat Rev Gastroenterol Hepatol*. 2020;17(9):557-588. doi:10.1038/s41575-020-0310-z
14. Broomé U, Olsson R, Lööf L, et al. Natural history and prognostic factors in 305 Swedish patients with primary sclerosing cholangitis. *Gut*. 1996;38(4):610-615. doi:10.1136/gut.38.4.610
15. Patel N, Benipal B. Incidence of Cholangiocarcinoma in the USA from 2001 to 2015: A US Cancer Statistics Analysis of 50 States. *Cureus*. 2019;11(1):e3962. Published 2019 Jan 25. doi:10.7759/cureus.3962
16. Saha SK, Zhu AX, Fuchs CS, Brooks GA. Forty-Year Trends in Cholangiocarcinoma Incidence in the U.S.: Intrahepatic Disease on the Rise. *Oncologist*. 2016;21(5):594-599. doi:10.1634/theoncologist.2015-0446
17. Clements O, Eliahoo J, Kim JU, Taylor-Robinson SD, Khan SA. Risk factors for intrahepatic and extrahepatic cholangiocarcinoma: A systematic review and meta-analysis. *J Hepatol*. 2020;72(1):95-103. doi:10.1016/j.jhep.2019.09.007
18. Razumilava N, Gores GJ, Lindor KD. Cancer surveillance in patients with primary sclerosing cholangitis. *Hepatology*. 2011;54(5):1842-1852. doi:10.1002/hep.24570

19. Walpole S, Pritchard AL, Cebulla CM, et al. Comprehensive Study of the Clinical Phenotype of Germline BAP1 Variant-Carrying Families Worldwide. *J Natl Cancer Inst*. 2018;110(12):1328-1341. doi:10.1093/jnci/djy171
20. Yeung YP, AhChong K, Chung CK, Chun AY. Biliary papillomatosis: report of seven cases and review of English literature. *J Hepatobiliary Pancreat Surg*. 2003;10(5):390-395. doi:10.1007/s00534-002-0837-0
21. Nakeeb A, Pitt HA, Sohn TA, et al. Cholangiocarcinoma. A spectrum of intrahepatic, perihilar, and distal tumors. *Ann Surg*. 1996;224(4):463-475. doi:10.1097/00000658-199610000-00005
22. Sinakos E, Saenger AK, Keach J, Kim WR, Lindor KD. Many patients with primary sclerosing cholangitis and increased serum levels of carbohydrate antigen 19-9 do not have cholangiocarcinoma. *Clin Gastroenterol Hepatol*. 2011;9(5):434-9.e1. doi:10.1016/j.cgh.2011.02.007
23. Zhang BH, Yang BH, Tang ZY. Randomized controlled trial of screening for hepatocellular carcinoma. *J Cancer Res Clin Oncol*. 2004;130(7):417-422. doi:10.1007/s00432-004-0552-0
24. Fadahunsi OO, Ibitoye BO, Adisa AO, Alatise OI, Adetiloye VA, Idowu BM. Diagnostic accuracy of ultrasonography in adults with obstructive jaundice. *J Ultrason*. 2020;20(81):e100-e105. doi:10.15557/JoU.2020.0016
25. Sharma MP, Ahuja V. Aetiological spectrum of obstructive jaundice and diagnostic ability of ultrasonography: a clinician's perspective. *Trop Gastroenterol*. 1999;20(4):167-169.
26. Razumilava N, Gores GJ, Lindor KD. Cancer surveillance in patients with primary sclerosing cholangitis. *Hepatology*. 2011;54(5):1842-1852. doi:10.1002/hep.24570
27. Schellhaas B, Wildner D, Pfeifer L, et al. LI-RADS-CEUS - Proposal for a Contrast-Enhanced Ultrasound Algorithm for the Diagnosis of Hepatocellular Carcinoma in High-Risk Populations. LI-RADS-CEUS mit kontrastverstärktem Ultraschall – Vorschlag für eine standardisierte Klassifikation HCC-suspekter Leberraumforderungen bei Risikopatienten. *Ultraschall Med*. 2016;37(6):627-634. doi:10.1055/s-0042-112221
28. Freitas PS, Janicas C, Veiga J, Matos AP, Herédia V, Ramalho M. Imaging evaluation of the liver in oncology patients: A comparison of techniques. *World J Hepatol*. 2021;13(12):1936-1955. doi:10.4254/wjh.v13.i12.1936
29. Choi SH, Han JK, Lee JM, et al. Differentiating malignant from benign common bile duct stricture with multiphasic helical CT. *Radiology*. 2005;236(1):178-183. doi:10.1148/radiol.2361040792
30. Iavarone M, Piscaglia F, Vavassori S, et al. Contrast enhanced CT-scan to diagnose intrahepatic cholangiocarcinoma in patients with cirrhosis. *J Hepatol*. 2013;58(6):1188-1193. doi:10.1016/j.jhep.2013.02.013
31. Fowler KJ, Sheybani A, Parker RA 3rd, et al. Combined hepatocellular and cholangiocarcinoma (biphenotypic) tumors: imaging features and diagnostic accuracy of contrast-enhanced CT and MRI. *AJR Am J Roentgenol*. 2013;201(2):332-339. doi:10.2214/AJR.12.9488
32. Olthof SC, Othman A, Clasen S, Schraml C, Nikolaou K, Bongers M. Imaging of Cholangiocarcinoma. *Visc Med*. 2016;32(6):402-410. doi:10.1159/000453009
33. Lowe RC, Anderson CD, Kowdley KV. Clinical manifestations and diagnosis of cholangiocarcinoma. In: Post TW, ed. *UpToDate*. UpToDate; 2023. Accessed September 27, 2023. https://www-uptodate-com
34. van der Pol CB, McInnes MDF, Salameh JP, et al. CT/MRI and CEUS LI-RADS Major Features Association with Hepatocellular Carcinoma: Individual Patient Data Meta-Analysis [published correction appears in Radiology. 2023 Apr;307(1):e239005]. *Radiology*. 2022;302(2):326-335. doi:10.1148/radiol.2021211244
35. Khan SA, Davidson BR, Goldin RD, et al. Guidelines for the diagnosis and treatment of cholangiocarcinoma: an update. *Gut*. 2012;61(12):1657-1669. doi:10.1136/gutjnl-2011-301748
36. Sahani D, Mehta A, Blake M, Prasad S, Harris G, Saini S. Preoperative hepatic vascular evaluation with CT and MR angiography: implications for surgery. *Radiographics*. 2004;24(5):1367-1380. doi:10.1148/rg.245035224
37. Yeh TS, Jan YY, Tseng JH, et al. Malignant perihilar biliary obstruction: magnetic resonance cholangiopancreatographic findings. *Am J Gastroenterol*. 2000;95(2):432-440. doi:10.1111/j.1572-0241.2000.01763.x
38. Park HS, Lee JM, Choi JY, et al. Preoperative evaluation of bile duct cancer: MRI combined with MR cholangiopancreatography versus MDCT with direct cholangiography. *AJR Am J Roentgenol*. 2008;190(2):396-405. doi:10.2214/AJR.07.2310
39. Manfredi R, Barbaro B, Masselli G, Vecchioli A, Marano P. Magnetic resonance imaging of cholangiocarcinoma. *Semin Liver Dis*. 2004;24(2):155-164. doi:10.1055/s-2004-828892
40. Chong YS, Kim YK, Lee MW, et al. Differentiating mass-forming intrahepatic cholangiocarcinoma from atypical hepatocellular carcinoma using gadoxetic acid-enhanced MRI. *Clin Radiol*. 2012;67(8):766-773. doi:10.1016/j.crad.2012.01.004
41. Forner A, Vidili G, Rengo M, Bujanda L, Ponz-Sarvisé M, Lamarca A. Clinical presentation, diagnosis and staging of cholangiocarcinoma. *Liver Int*. 2019;39 Suppl 1:98-107. doi:10.1111/liv.14086
42. National Comprehensive Cancer Network. Biliary Tract Cancers (Version 1.2022). NCCN Clinical Practice Guidelines in Oncology. https://www.nccn.org/professionals/physician_gls/pdf/btc.pdf. Published January 19, 2022. Accessed February 1, 2024.
43. Primrose JN, Fox R, Palmer DH, Prasad R, Mirza D, Anthoney DA, et al. Adjuvant capecitabine for biliary tract cancer: The BILCAP randomized study. JCO. 2017;35: 4006–4006. https://doi.org/10.1200/JCO.2017.35.15_suppl.4006.
44. Oh DY, He AR, Qin S, et al. Durvalumab plus gemcitabine and cisplatin in advanced biliary tract cancer. NEJM Evid. 2022;1:EVID0a2200015. Available at: https://evidence.nejm.org/doi/full/10.1056/EVIDoa2200015
45. Kelley RK, Ueno M, Yoo C, et al. Pembrolizumab in combination with gemcitabine and cisplatin compared with gemcitabine and cisplatin alone for patients with advanced biliary tract cancer (KEYNOTE-966): A randomised, double-blind, placebo-controlled, phase 3 trial. Lancet. 2023;401:1853-1865. Available at: https://www.ncbi.nlm.nih.gov/pubmed/37075781.
46. Darwish Murad S, Kim WR, Harnois DM, et al. Efficacy of neoadjuvant chemoradiation, followed by liver transplantation, for perihilar cholangiocarcinoma at 12 US centers. *Gastroenterology*. 2012;143(1):88-e14. doi:10.1053/j.gastro.2012.04.008
47. Hoffmann RT, Paprottka PM, Schön A, et al. Transarterial hepatic yttrium-90 radioembolization in patients with unresectable intrahepatic cholangiocarcinoma: factors associated with prolonged survival. *Cardiovasc Intervent Radiol*. 2012;35(1):105-116. doi:10.1007/s00270-011-0142-x
48. Kim JH, Won HJ, Shin YM, Kim KA, Kim PN. Radiofrequency ablation for the treatment of primary intrahepatic cholangiocarcinoma. *AJR Am J Roentgenol*. 2011;196(2):W205-W209. doi:10.2214/AJR.10.4937

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Resilience Curriculum Improves Skills of Pediatric Fellows in Delivery of Difficult News

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ABSTRACT

BACKGROUND: Delivering difficult news to families is an essential but challenging skill. Pediatric trainees report limited confidence in this skill and perform poorly in simulation. We implemented the American Academy of Pediatrics (AAP) Resilience Curriculum and evaluated performance and self-efficacy in delivering difficult news.

METHODS: The AAP Resilience Curriculum, using the SPIKES (Set-up, Perception, Invitation, Knowledge, Empathy, and Summary) framework, was taught to pediatric fellows. Fellows' performance during simulations with standardized patients before and after curriculum implementation was scored with a SPIKES checklist. Pre- and post-test surveys assessed self-efficacy in delivering difficult news.

RESULTS: Fellows (n=19) significantly improved their performance in delivering difficult news, increasing the median SPIKES checklist scores from 78% to 90% completion (P<0.001). Pediatric fellows (n=35) reported improved confidence from 3.4/5 to 3.9 (P=0.01).

CONCLUSIONS: Pediatric fellows demonstrated significant improvement in their ability to deliver difficult news during a simulated patient encounter and reported increased self-efficacy in delivering difficult news.

KEYWORDS: medical education, difficult news, simulation, standardized patients, pediatric fellows

INTRODUCTION

Delivering difficult news, or "information likely to seriously affect the patient's view of their future," to families and their children is a universal experience in pediatrics.[1] As such, the Accreditation Council for Graduate Medical Education expects pediatric trainees to be competent in effective and empathic communication with patients and families.[2] A study by Sastre et al found that the patient acceptability of news disclosure was determined by the method of delivery – specifically, the quality of the information and emotional supportiveness — regardless of the seriousness of the news.[3] Despite the need for competent disclosure of information, clinicians report anxiety and dread when discussing serious diagnoses and death, with 86% of trainees in one study reporting some level of stress.[4] Physician apprehension in regard to this subject may, in part, be due to a lack of education, as pediatric trainees at all levels report minimal preparation for discussing bad news and life-threatening illness.[5-9]

To improve physician-patient communication in disclosing unfavorable information, several educational interventions have demonstrated improved self-efficacy or performance in simulation in delivering difficult news.[9-11] However, these interventions were largely locally developed and tested, without broad dissemination.[10-13] In 2016, an American Academy of Pediatrics (AAP) working group published the Resilience Curriculum prior to assessment of its impact to address pressing pediatric trainee educational needs, including delivery of difficult news.[14] The current study evaluated the AAP Resilience Curriculum's impact on pediatric subspecialty fellow performance and self-efficacy with delivering difficult news.

METHODS

Research Design

We implemented the AAP Resilience Curriculum, Part B, within the Yale Pediatric Fellowships Joint Curriculum as a two-part series.[15] We used a quantitative research design to asses both performance during the delivery of difficult news in a simulation by Observed Structured Clinical Examinations (OSCE) with a standardized patient and self-efficacy before and after the course. The study was deemed exempt from oversight by the Yale Institutional Review Board.

All 49 pediatric fellows in 11 pediatric fellowship programs within the Yale School of Medicine were eligible to participate, except for one fellow who led the study. Participation in OSCEs was not a prerequisite for participation in the educational activities. The study took place at Yale New Haven Children's Hospital, a 212-bed academic institution.

Curriculum Description

The AAP Resilience Curriculum (Part B) employs the SPIKES (Setup/Staging, Perception, Invitation, Knowledge, Empathy/Emotion, and Strategy/Summary) framework, initially developed in adult oncology by Baile and Buckman.[1,15] SPIKES provides a series of recommended steps to perform when disclosing difficult news to patients and families.

Pediatric fellows participated in the curriculum as part of their weekly one-hour multispecialty fellows' conference, taught by one of the investigators, TM. The first session introduced the SPIKES model through an interactive didactic and a role modeling demonstration, in which attending physicians acted out both an effective and a poor example of news delivery, notifying a parent of the unexpected death of their child. One month later, fellows participated in a second session of role plays and reflection.

Simulation Protocol

Prior to the implementation of the curriculum, we conducted pre-test OSCEs. We adapted two Resilience Curriculum role play scenarios into simulation cases. In each case, a child had died suddenly and unexpectedly from an accidental cause and the physician must inform a parent (SIDS Case) or a grandparent (Choking Case) that the child has died. Two standardized patients were hired and trained by TM and the Yale School of Medicine Teaching and Learning Center. During each session, the cases were alternated to ensure equal occurrence of each, and fellows were scheduled according to their availability. The post OSCE occurred two-three weeks after educational sessions were completed, three months after the pre-assessment. Post-test performance was assessed with the other case, not previously encountered by the participant. The simulations were videotaped for later evaluation. After completion of the post OSCE, the course instructor conducted a short individual debrief with each participant.

Data Collection and Assessment

Two different raters used two different measures to assess performance. An in-person research assistant rated fellows in real time, while sitting in the room during the OSCEs. Additionally, a trained fourth-year medicine-pediatrics resident reviewed the videos and scored performance post-hoc, blinded to whether data were from the pre- or post-test. They scored performance using a SPIKES checklist previously published by Tobler et al, which includes 17 items anchored on the SPIKES framework.[11] The items were scored as follows: 0 – not done or inadequate, 1 – adequate, and 2 – good. They also evaluated overall communication skill, using the Mini-Master Interview Rating Scale (MMIRS), shortened to nine questions from the full-length 27-question MIRS.[16] Drs. Talwalkar and Ellman and colleagues at the Yale School of Medicine previously developed the shortened version of the MIRS to test senior medical students in advanced communication OSCEs. The MMIRS was scored on a 5-point Likert scale, anchored on specific descriptions of behavior for each item.

Fellows rated their baseline self-efficacy with a survey immediately before the initial seminar. They completed post self-efficacy surveys immediately after the role play session. Demographic information collected included post-graduate year (PGY) of training, gender, age, previous training in delivering difficult news, and location of that training. A 13-question survey assessed self-efficacy, also previously published by Tobler et al.[11] We expanded the survey stem to ask participants to rate the domains of knowledge, confidence, and comfort separately for each item. The items themselves were unchanged. Fellows scored themselves on a Likert scale of 1 to 5, with 1 – strongly disagree to 5 – strongly agree, for each item in each domain.

Analysis

The SPIKES checklist percentages and MMIRS average score for the pre- and post-OSCEs were analyzed by the Wilcoxon signed rank test. Factors that could impact the outcome, including age, gender, PGY, prior training, and OSCE case 1 versus case 2, were analyzed using the Pearson correlation coefficient. The agreement between raters was evaluated using intraclass correlation coefficient. The relationship between performance and self-efficacy was analyzed using the Pearson correlation coefficient. For all analyses, the level of significance was set for 0.05. Analysis was conducted using SPPS version 24.0.

RESULTS

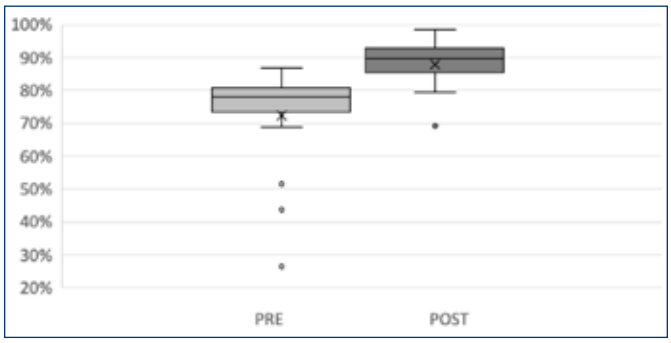
Performance in Simulation

Of 48 eligible subjects, 24 volunteered for the simulations, forming the simulation cohort. Given scheduling constraints, 21 completed the pre OSCE and 22 completed the post OSCE, with 19 finishing both pre- and post-OSCEs. Of the 19 paired assessments, the pre-test median completion of the SPIKES checklist significantly rose from 78% to 90% (Inter-quartile range [IQR] pre: 75–81%, post: 85–92%; p-value [*P*]<0.001; **Figure 1A**). The MMIRS pre-test group median of individual average scores significantly increased from 4.2 to 4.6 (IQR pre: 4.0–4.3, post: 4.4–4.7; p<0.001; **Figure 1B**). Gender, PGY, prior training, and OSCE case did not significantly correlate with the outcome. The inter-rater agreement was moderate for both metrics, with intra-class correlation (ICC) for absolute agreement and consistency for SPIKES of 0.69, and 0.72, respectively.[17] The MMIRS ICCs were 0.67, and 0.72, respectively. In the debriefing following the post-test OSCE, fellows universally expressed appreciation for the opportunity to practice delivering difficult news with standardized patients, instead of with real patients.

Self-Efficacy

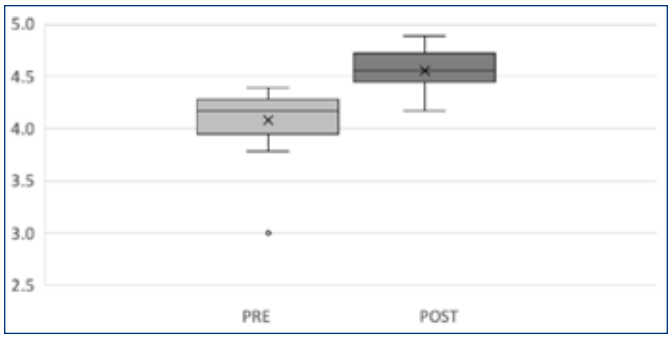
Knowledge, confidence, and comfort in delivering difficult news increased significantly for the 35 fellows who completed the self-efficacy survey during participation in the didactics. Knowledge increased significantly from a mean of 3.5/5 to 4.2 (Confidence interval [CI] pre: 3.4–3.7, post: 4–4.4; $P \leq 0.001$), confidence rose from 3.4 to 3.9 (CI pre: 3.2–3.6, post: 3.7–4.0; $P=0.01$), and comfort improved from 3.3

Figure 1A. Distribution of Fellow Simulation Performance
SPIKES Checklist Percentage Complete (n=19)



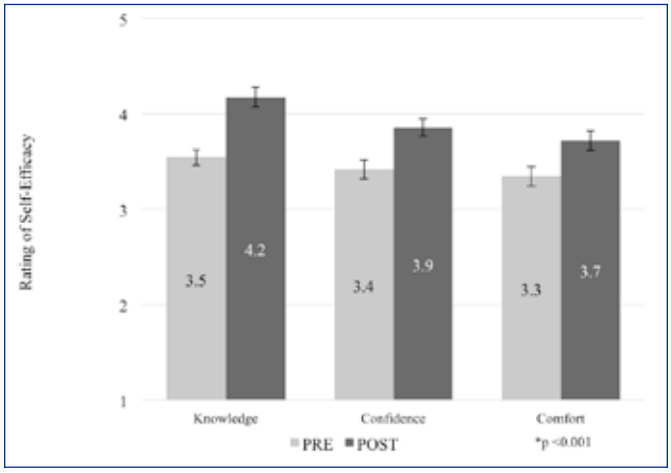
The SPIKES checklist (A) contains 17 items, anchored on behaviors in the SPIKES framework. It is scored: 0 – not done, 1 – partially done, and 2 – done well. There was a statistically significant difference between pre- and post-testing.

Figure 1B. MMIRS Average Composite Score (n=19)



The MMIRS (B) contains 9 items scored on a 5-point Likert scale rating communication during patient-centered interviewing. The median for the group is displayed above. There was a statistically significant difference between pre- and post-testing.

Figure 2. Self-Efficacy of Trainees in Delivering Difficult News (n = 35)



The self-efficacy survey consisted of 13 questions regarding different aspects of delivering difficult news. Each item was scored on a Likert scale of 1 to 5, with 1 – strongly disagree, to 3 – cannot agree or disagree, to 5 – strongly agree. An average score for each domain, of knowledge, confidence, and comfort was calculated for the group.

to 3.7 (CI pre: 3.2–3.5, post: 3.5–3.9; $P<0.01$). When plotting the change in specific individuals, it was noted that a few demonstrated a decrease in self-efficacy from pre- to post-test (**Figure 2**). Additionally, when analyzing different types of communication skills within delivering difficult news, it was noted that trainees report more comfort with items related to displaying empathy than with those pertaining to managing emotions.

Performance and Self-Efficacy

Twenty (20) of the 24 fellows from the simulation cohort had a self-efficacy survey to pair with their simulation performance data from either pre-didactic, post-didactic, or both. Their self-efficacy data were compared to their performance in the simulations and it was found that the SPIKES checklist score significantly correlated with the total self-efficacy score (R = 0.396, $P=0.011$) on both pre- and post-data sets, although it is a weak to moderate positive relationship. The MMIRS score correlation with self-efficacy approached, but did not cross, the threshold for significance (R = 0.312, $P=0.050$).

DISCUSSION

The significant improvement in performance and reported self-efficacy of pediatric fellows demonstrates the promise of effectiveness of the AAP Resilience Curriculum at advancing the preparation of pediatric fellows for delivering difficult news to patients and families. To our knowledge, the current study is the first to validate the AAP Resilience Curriculum. This nationally available curriculum provides open access to a toolkit that can be adapted to meet local communication training needs.[15]

Unexpectedly, prior training did not have a significant impact on performance, a minority of individuals reported decreased self-efficacy following training, and performance and self-efficacy were correlated. The finding that prior training did not significantly impact the baseline performance of fellows indicates either a decay in the effect of such prior training – given that most reported training occurred in medical school – or lack of effectiveness of the training received. Admittedly, this study was underpowered to detect the impact of prior training on performance.

The decrease in self-efficacy from pre- to post-test may be due to the Dunning-Kruger phenomena of poor insight in the unskilled, whereby "paradoxically, improving the skills of participants, and thus increasing their metacognitive competence, helped them recognize the limitations of their abilities."[18] These individuals may have been overly confident in their skills in delivery of difficult news, and, after receiving training and reflecting on their own skills, realized that they were not as prepared as they had initially thought. Additionally, this phenomenon may also explain why prior

training did not have a significant impact, as those with more training may have better recognition of what they lack.

In counterpoint to those individuals with poor initial insight that improves with education, the correlation between performance and self-efficacy among the fellows is notable. Self-efficacy is generally considered a less robust measure of educational effectiveness according to Kirkpatrick's Model, and physicians have been shown to be poor self-assessors.[19,20] However, this correlation indicates some merit in using self-efficacy as a measure of curricular assessment for education, potentially specific to communication skills. Additionally, given the considerable stress experienced by trainees when delivering difficult news, self-efficacy may impact communication skill acquisition.[4] As such, an intervention that results in increased confidence and comfort is valuable.

Modifying the curriculum using simulation added value to the learners, as they unanimously expressed their appreciation for the opportunity to practice giving difficult news to a standardized patient in the lower stakes environment of simulation. Further, in regard to trainee needs, it is notable that participants report the lowest self-efficacy in managing emotions when delivering difficult news. This finding suggests that implementation of this curriculum should explicitly address and expand upon the emotionally challenging aspects of delivering difficult news while teaching the SPIKES model, which is available in other portions of the Resilience Curriculum.

This study was limited by the single center design and by the fact that individuals self-selected to participate. This potential selection bias may have influenced the results by including more engaged and motivated learners. Additionally, participation was impacted by trainee schedules. The inherent challenge of full saturation of a curriculum among busy trainees may be addressed by including this training in orientation, or by using previously protected didactic time for the simulation portion of the curriculum. Finally, we do not know if these effects in simulation translate into improved delivery of difficult news to patients and their families. Further study into how this training affects the actual experience of families may be amenable to qualitative study.

CONCLUSION

Pediatric trainees demonstrated significant improvements in observable skill and self-efficacy in delivering difficult news after participation in a course based on the AAP Resiliency Curriculum. Continuation of this curriculum in the annual fellowship curriculum is essential. Additionally, implementation of similar didactic and simulation-based curricula at the regional level during pediatric critical care medicine bootcamps could serve to start addressing a critical deficit in pediatric subspecialty training.

References

1. Baile WF, Buckman R, Lenzi R, et al. SPIKES-A six-step protocol for delivering bad news: application to the patient with cancer. *Oncologist.* 2000;5:302-311.
2. Benson BJ. Domain of competence: Interpersonal and communication skills. *Acad Pediatr.* 2014;14: S55-65. DOI: 10.1016/j.acap.2013.11.016.
3. Sastre MTM, Sorum PC, Mullet E. Breaking Bad News: The Patient's Viewpoint. *Health Commun.* 2011;26: 649-655. DOI: 10.1080/10410236.2011.561919.
4. Shaw JM, Brown RF, Dunn SM. A qualitative study of stress and coping responses in doctors breaking bad news. *Patient Educ Couns.* 2013;91:243-248. 2012/12/05. DOI: 10.1016/j.pec.2012.11.006.
5. Johnson EM, Hamilton MF, Watson RS, et al. An Intensive, Simulation-Based Communication Course for Pediatric Critical Care Medicine Fellows. *Pediatr Crit Care Med.* 2017;18: e348-e355. DOI: 10.1097/PCC.0000000000001241.
6. Kolarik RC, Walker G, Arnold RM. Pediatric resident education in palliative care: a needs assessment. *Pediatrics.* 2006;117:1949-1954. DOI: 10.1542/peds.2005-1111.
7. Arnold RM, Back AL, Barnato AE, et al. The Critical Care Communication project: improving fellows' communication skills. *J Crit Care.* 2015;30:250-254. DOI: 10.1016/j.jcrc.2014.11.016.
8. Rider EA, Volkan K, Hafler JP. Pediatric residents' perceptions of communication competencies: Implications for teaching. *Med Teach.* 2008;30: e208-217. 2008/09/09. DOI: 10.1080/01421590802208842.
9. Reed S, Kassis K, Nagel R, et al. Breaking bad news is a teachable skill in pediatric residents: A feasibility study of an educational intervention. *Patient Educ Couns.* 2015; 98:748-752. DOI: 10.1016/j.pec.2015.02.015.
10. Greenberg LW, Ochsenschlager D, O'Donnell R, et al. Communicating bad news: a pediatric department's evaluation of a simulated intervention. *Pediatrics.* 1999;103:1210-1217.
11. Tobler K, Grant E, Marczinski C. Evaluation of the impact of a simulation-enhanced breaking bad news workshop in pediatrics. *Simul Healthc* 2014;9:213-219. DOI: 10.1097/SIH.0000000000000031.
12. Chumpitazi CE, Rees CA, Chumpitazi BP, et al. Creation and Assessment of a Bad News Delivery Simulation Curriculum for Pediatric Emergency Medicine Fellows. *Cureus.* 2016;8: e595. DOI: 10.7759/cureus.595.
13. Wolfe AD DS, Baker J, Catrine K, Hoover-Regan M. Bad news deserves better communication: a customizable curriculum for teaching learners to share life-altering information in pediatrics. MedEdPORTAL Publications, 2016.
14. Serwint JR, Bostwick S, Burke AE, et al. The AAP Resilience in the Face of Grief and Loss Curriculum. *Pediatrics* 2016;138. DOI: 10.1542/peds.2016-0791.
15. Resilience Curriculum: Resilience in the face of grief and loss, https://www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/hospice-palliative-care/Pages/Resilience-Curriculum.aspx (accessed 3/2/17 2017).
16. Stillman PL, Brown DR, Redfield DL, et al. Construct-Validation of Arizona Clinical Interview Rating-Scale. *Educ Psychol Meas.* 1977;37:1031-1038. DOI: Doi 10.1177/001316447703700427.
17. Koo TK, Li MY. A Guideline of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research. *J Chiropr Med.* 2016;15:155-163. 2016/06/23. DOI: 10.1016/j.jcm.2016.02.012.
18. Kruger J, Dunning D. Unskilled and unaware of it: how difficulties in recognizing one's own incompetence lead to inflated self-assessments. *J Pers Soc Psychol.* 1999;77:1121-1134. 2000/01/08.
19. Davis DA, Mazmanian PE, Fordis M, et al. Accuracy of physician self-assessment compared with observed measures of competence: a systematic review. *JAMA*. 2006;296:1094-1102. 2006/09/07. DOI: 10.1001/jama.296.9.1094.
20. Kirkpatrick JD, Kirkpatrick WK. *Kirkpatrick's four levels of training evaluation*. Alexandria, VA: ATD Press, 2016, p.xviii, 238 pages.

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IHCME

Estimating the Effectiveness of COVID-19 Mitigation Policy in Rhode Island

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BACKGROUND

When the first cases of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) were detected in Rhode Island in late February 2020, little was known about the disease, except that it was a coronavirus to which the entire human population was immunologically naive, that its basic reproduction number was between 1.4 and 2.5,[1] and that it had the potential of causing severe respiratory symptoms and death in sufficient proportions to overwhelm hospital systems quickly. At that moment, Rhode Island, like many other jurisdictions in the United States, had two significant vulnerabilities: tight limits on its ability to expand hospital bed capacity beyond existing demands, and a very limited stockpile of personal protective equipment for hospital personnel.[2,3] Given this situation, the state implemented strict mitigation interventions in real time to slow disease transmission.

Given all the unknowns posed by a novel virus, combined with daily reports of mounting disease burden in China[4] and the urgency inherent in the World Health Organization's official declaration of pandemic (March 11, 2020),[5] the only sure mitigative tool in public health's armamentarium to minimize disease exposure in the general population was a blunt one: reduction in the density of the general population by sheltering in place (what became known around the world colloquially as "lockdown"[6]). Accordingly, in a mere two weeks (March 9–22, 2020) the Governor of Rhode Island shut down most indoor public venues – schools, churches, sports events, theatrical events, bars and restaurants, densely populated workplaces, etc. – and limited the size of social gatherings in all settings to 25 people.[7] Other tweaks of Rhode Island's policy package would follow, such as an order for "employees at 'customer-facing' businesses to wear masks,"[7] 14-day quarantines for travelers entering the state, and temporary closures of outdoor public venues such as beaches and parks,[7] but by March 23, 2020, the density and mixing of the general public in Rhode Island was about as minimal as possible under the circumstances. Rhode Island would remain in this state for seven weeks, at which time restrictions on the size of social gatherings were eased slightly in what was called "Phase One of Reopening,"[7] beginning May 9, 2020. Phases 2 and 3 would follow on June 1 and 30, 2020, respectively, effectively allowing most businesses to reopen, subject to rules such as masking.[7] In September, most Rhode Island schools at all levels would reopen for in-person instruction.[7]

The closures and other restrictive policies of early 2020 produced undesirable effects, primarily on employment and schooling. Thousands of Rhode Island workers were laid off in March 2020 as workplaces shut down,[8] and Rhode Island students at all levels were transitioned from classroom to remote learning.[7] Most people became more socially isolated than they had ever been. It will require years of research to understand all the negative consequences of the blunt mitigative tools applied (worldwide) in early 2020. However, the positive consequences – reductions in potential morbidity and mortality – may be explored with epidemic models, and this is what we set out to do, using simple epidemic models to compare the results of two hypothetical scenarios with the observed burden of COVID-19 in Rhode Island during the first year of the pandemic.

METHODS

First, a simple S-I-R approach was used to model the first epidemic year of the Coronavirus Disease of 2019 (COVID-19) in Rhode Island, 1/27/2020–2/28/2021, using counts of hospital admissions as the primary basis of the models, supplemented by counts of positive tests and deaths when these data became available and were deemed reliable.

The S-I-R model, introduced to epidemiology a century ago,[9] models epidemics mechanistically, by describing them as the outcome of a stylized infection process on homogeneous groups of people. In the simplest form of this model, a susceptible group (S) may be infected upon contact with people in an infectious group (I), who will in turn recover or die and move to a "removed" group (R). The advantage of this stylized model is that it is easy to conceptualize, it is transparent, and it is easily replicable, because it is fully described by a set of simple algebraic (difference) equations. In its deterministic implementation, which ignores complicated descriptions of uncertainty, one can easily explore the impact of parameter changes on results.

To tailor an S-I-R model to Rhode Island, we used a total population size of 1,097,379 people, the 2020 U.S. Census count for Rhode Island,[10] a disease duration of D = 10 days, and a reproduction number at the beginning of the epidemic of R(0) = 2.5. The reproduction number, R(t), where t refers

to the "epidemic day" from 0 to N, the end of the epidemic, is the average number of new infections that each infectious person generates over the duration of their illness. R(0) is called the "basic reproduction number," while R(>0), e.g., R(1), R(2), R(3)…, is called the "effective reproduction number." The values we used for D and R(0) are within accepted ranges for the original strain of SARS-CoV-2.[11]

R(t) depends on many factors, including characteristics of the pathogen, the proportion of the population in the susceptible group, and how likely it is that an infectious and a susceptible person will interact closely enough for the latter to be infected. Infections are more likely to occur when there is a higher "density of interactions." Therefore, as a population becomes denser, R(t) increases; as it becomes less dense, R(t) decreases.

Daily new hospital admissions (hospitalizations) were modeled by assuming ratios of hospitalizations to our model's estimates of daily underlying infections as follows: 5% from 2/27/2020 through 5/31/2020, during a period of nursing home outbreaks, a 45-day transition from 5% to 3% as nursing home outbreaks were brought under control, and 3% thereafter. These Rhode Island-specific ratios were estimated by the Rhode Island Pandemic Modeling Team (RIPMT) in 2020 and have been working well during the four continuous years of COVID-19 monitoring. (JF, TT, and JP have been core members of the RIPMT from its inception.)

Deaths were modeled by applying observed ratios of deaths to hospitalizations as follows: 50% from 2/27/2020 through 5/31/2020, a 10-day transition from 50% to 25%, and 25% thereafter.

The model was then conformed to empirical observations by scaling the daily effective reproduction number, R(t), by a factor representing daily relative population density, d(t), permitted to vary between 1 (normal density) and 0 (a theoretical impossibility in which all members of the population are isolated from one another) (**Figure 1**). A daily value of d(t) was estimated such that daily hospitalizations resulting from the S-I-R model conformed to observed daily hospitalizations within about ± 10%. (The resulting "fit" is plotted in **Figure 2**.)

By plotting d(t), we were able to see and interpret the effects of mitigative public health policy as applied to reduce population density (to retard disease transmission) or removed to permit a return to normal population density. d(t) also reveals periods in which population density is naturally reduced (e.g., during summer months) and naturally increased (e.g., return to school in late summer and the holiday season at year's end) (**Figure 1**).

Then, two hypothetical scenarios were run:

Scenario 1 (S1): laissez-faire policy, in which the initial reduction in d(t) is limited to half of the observed reduction, i.e., 25% vs. 50%, simulating voluntary reduction in population density, e.g., voluntary actions to shelter in place, followed by the same seasonal pattern in d(t) as the empirical model, followed by voluntary reductions in the number and size of holiday gatherings (**Figure 3**).

Scenario 2 (S2): absence of policy, in which observed reductions in d(t) are eliminated except for seasonal (summer and fall) variations in d(t), to simulate the full potential of an R(0) = 2.5 epidemic, i.e., a theoretical, disastrous extreme in which people do not self-quarantine or otherwise adjust their behavior during the epidemic (**Figure 4**).

Figure 1. Estimated Proportionate Population Density, *Derived* (Rhode Island, 2/27/2020–2/28/2021)

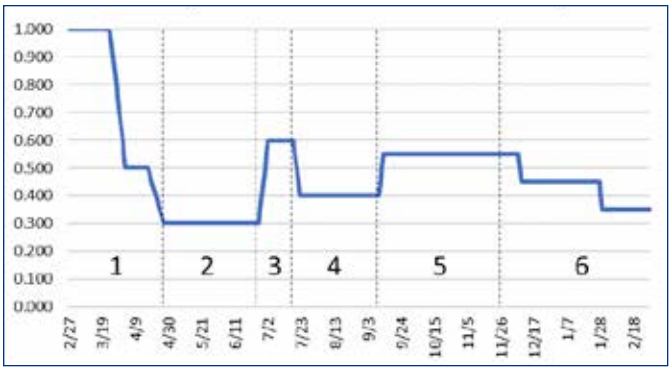


Figure 2. Hospital Admissions: Modeled and Observed (Rhode Island, 2/27/2020–2/28/2021)

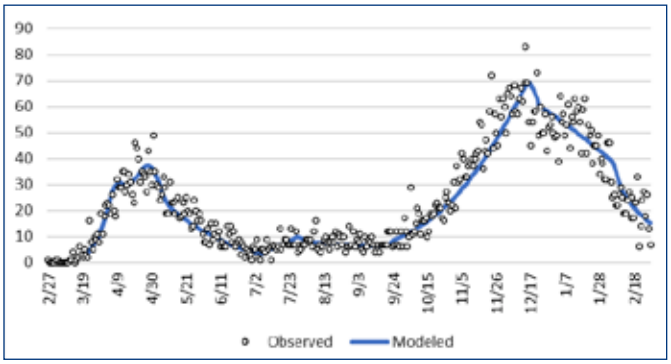


Figure 3. Modeled Proportionate Population Density, *Scenario 1* (Rhode Island, 2/27/2020–2/28/2021)

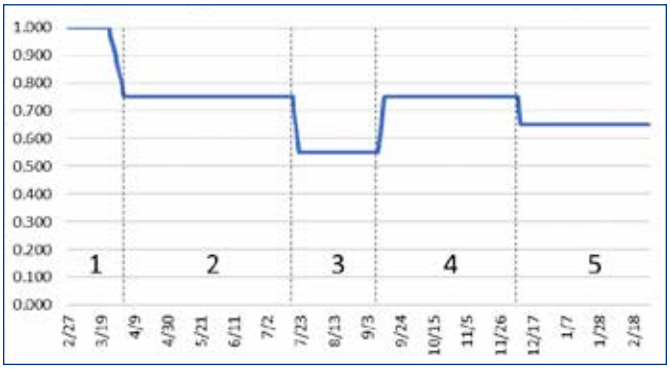


Figure 4. Estimated Proportionate Population Density, *Scenario 2* (Rhode Island, 2/27/2020–2/28/2021)

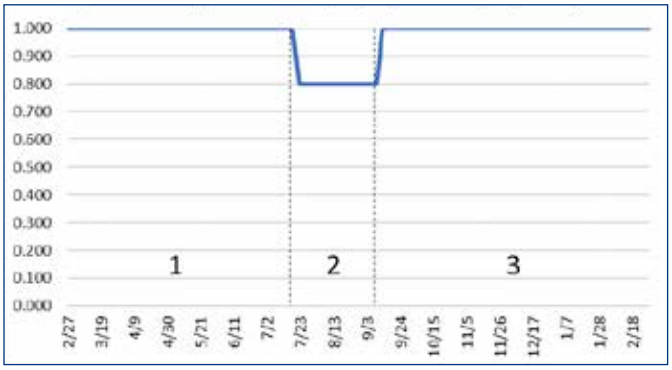


Figure 5. Hospital Admissions: Observed and Scenarios (Rhode Island, 2/27/2020–2/28/2021)

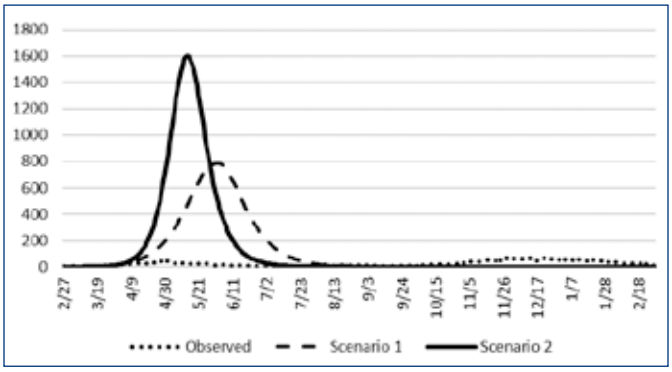
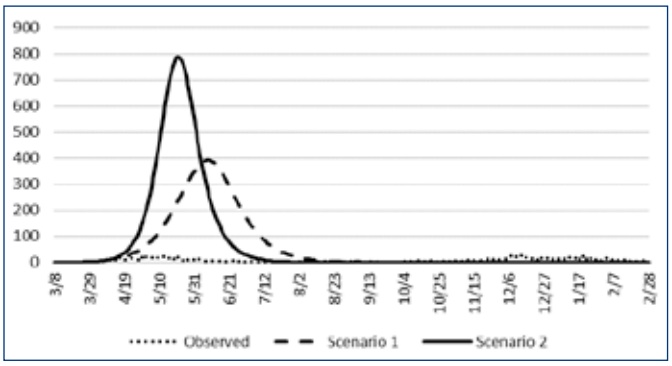


Figure 6. Deaths: Observed and Scenarios (Rhode Island, 2/27/2020–2/28/2021)



RESULTS

When the model is conformed to empirical reality, the revealed trend in d(t) has six distinct periods (**Figure 1**) related to pandemic policy and seasonal rhythms in population density: (1) lockdown; (2) stasis; (3) mitigative loosening; (4) reduction in the size of gatherings and summer's population decompression; (5) fall's recompression (return to school, work); (6) mitigative tightening in response to surging cases.[7] **Figure 2** reveals a good fit between observed and modeled hospitalizations when d(t) is derived in this way.

In S1 (**Figure 3**), the proposed trend in d(t) has five periods: (1) initial recommendations; (2) stasis; (3) summer's population decompression; (4) fall's population recompression; (5) holiday recommendations. In S2 (**Figure 4**), the proposed trend in d(t) has three periods: (1) normal population density; (2) summer's population decompression; (3) fall's population recompression.

S1 and S2 yield many more hospitalizations (H's) and deaths (D's) than observed in reality from 1/27/2020 through 2/28/2021. Voluntary mitigation (hypothetical scenario S1 – **Figure 5**) yields 30,361 (353%) more hospitalizations and 16,879 (648%) more deaths than enforced mitigation as implemented in Rhode Island. No mitigation (hypothetical scenario S2 – **Figure 6**) yields 40,367 (648%) more hospitalizations and 21,837 (839%) more deaths than enforced mitigation.

DISCUSSION

Despite being formulated during an intense public-health emergency, it is quite clear that improvised policies worked "to flatten the curve" in Rhode Island. Two possible "what ifs" reveal stark differences between what actually occurred in Rhode Island during the first year of COVID-19, what might have occurred with a hypothetical laissez-faire policy (S1), and the theoretical limits of epidemic morbidity and mortality without mitigation (S2).

Simple, transparent, and easily replicable S-I-R models suggest that SARS-CoV-2 hospitalizations might have been four to five times higher and deaths seven to eight times higher under the hypothetical laissez-faire policy we have characterized (S1) than observed under lockdown. Furthermore, the S1 hospitalization curve observed in **Figure 5** – together with what we know of the average length of stay of SARS-CoV-2 patients (10+ days well into July)[12] – suggests that Rhode Island's hospital system, whose maximum bed capacity at the time was 2,740,[13] would have been inundated with SARS-CoV-2 patients sometime in April, if not before. Just such a situation was playing out at the time in Italy,[14] whose COVID-19 epidemic surged well beyond the Rhode Island experience before the Italian government imposed a lockdown, as well. An even more sobering thought is that our S1 estimates of deaths (based on the empirical ratio of deaths to hospitalizations observed at the time) are clearly underestimates, for had the hospital system become dysfunctional, the death rate from other diseases and conditions requiring hospital care most likely would have increased as well.[15]

By flattening the curve of COVID-19 in Rhode Island, the state's enforced mitigative policies also reduced disease transmission before FDA emergency-use authorizations (EUAs) for remdesivir (antiviral) in May 2020,[16] of bamlanivimab (monoclonal antibody) in November,[17] and

of Pfizer-BioNTech COVID-19 vaccine in December.[18] Together, these advancements saved many lives by preventing or reducing the severity of SARS-CoV-2 infection. Others (e.g., casirivimab + imdevimab[19]) would follow in short order.

Variations of the S-I-R model were in common use during the COVID-19 pandemic. A simple search of publications with the terms "S-I-R model" and "COVID 19" yields thousands of references. The model has strengths and weaknesses,[20-22] but its venerable history, simplicity, transparency, and replicability render it useful in conducting hypothetical exercises such as the one we have conducted.

Similar exercises have been undertaken to assess the effects of policies designed "to flatten the curve" of COVID-19,[23-26] but none to date for Rhode Island. Our results, which clearly suggest the effectiveness of the state's enforced mitigative policies, provide a basis for a more detailed analysis of the effectiveness of individual policies employed at the time.

CONCLUSIONS

The closure of Rhode Island's schools and many Rhode Island businesses in 2020, despite untoward side effects, probably prevented upwards of 30,000 hospitalizations and 16,000 deaths (compared to a hypothetical laissez-faire policy), saved its hospital system from dysfunction, and pushed the epidemic forward in time, when antivirals, monoclonal antibodies, and vaccines became available to prevent disease and blunt its severity.

References

1. Statement on the meeting of the International Health Regulations (2005) Emergency Committee regarding the outbreak of novel coronavirus 2019 (n-CoV) on 23 January 2020. Geneva, Switzerland: World Health Organization, January 2020. https://www.who.int/news/item/23-01-2020-statement-on-the-meeting-of-the-international-health-regulations-(2005)-emergency-committee-regarding-the-outbreak-of-novel-coronavirus-(2019-ncov)
2. Grimm CA. Hospital experiences responding to the COVID-19 pandemic: results of a national pulse survey March 23–27, 2020. Washington, D.C.: US Department of Health and Human Services Office of Inspector General, April 2020. https://justthenews.com/sites/default/files/2020-04/HHS2020ReportPandemicHospitals.pdf
3. Personal communication from Alysia Mihalakos, Chief, Center for Emergency Preparedness and Response · Rhode Island Department of Health. March 2020.
4. Coronavirus disease 2019 (COVID-19): situation report, 31. Data as reported by 20 February 2020. Geneva, Switzerland: World Health Organization, February 2020. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200220-sitrep-31-covid-19.pdf
5. Coronavirus disease (COVID-19) pandemic. "Overview." Geneva, Switzerland: World Health Organization, 2020. https://www.who.int/europe/emergencies/situations/covid-19
6. Callaway E, Ledford H, Viglione G, Watson T, Witze A. COVID and 2020: An extraordinary year for science. Nature 2020. Published online. https://www.nature.com/immersive/d41586-020-03437-4/index.html
7. Journal Staff. Timeline of RI's COVID milestones. The Providence Journal, February 2021. https://www.providencejournal.com/story/news/healthcare/ 2021/02/25/rhode-island-coronavirus-timeline/4564028001/
8. Sherman E. COVID-19 unemployment claims top 10,000 in RI in less than a week. WPRI.com, March 17, 2020. https://www.wpri.com/health/coronavirus/covid-19-unemployment-claims-top-10000-in-ri-in-less-than-a-week/
9. Kermack WO, McKendrick AG. A contribution to the mathematical theory of epidemics. Proceedings of the Royal Society of London. Series A, Containing papers of a mathematical and physical character, 1927;115(772):700-721
10. State Profiles. Rhode Island. Suitland, Maryland U.S. Census Bureau, April 2024. https://data.census.gov/profile/Rhode_Island?g=040XX00US44
11. Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19) Geneva, Switzerland: World Health Organization, February 2020. https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf
12. State of Rhode Island. COVID-19 Rhode Island Data Archive. Accessed April 15, 2023. https://docs.google.com/spreadsheets/d/1c2QrNMz8pIbYEKzMJL7Uh2dtThOJa2j1sSMwiDo5Gz4/edit#gid=264100583
13. Personal communication from Dawn Lewis, Healthcare Emergency Management Director, Hospital Association of Rhode Island, August 25, 2020. Current staffed beds: 2436, from Statistics for Non-Federal, Short-Term, Acute Care Hospitals. Individual Hospital Statistics for Rhode Island. American Hospital Registry. Accessed April 25, 2024. https://www.ahd.com/states/hospital_RI.html
14. Paterlini M. On the front lines of coronavirus: the Italian response to covid-19. BMJ 2020;368: m1065 https://www.bmj.com/content/368/bmj.m1065
15. Luck AN, Stokes AC, Hempstead K, et al. Associations between mortality from COVID-19 and other causes: A state-level analysis. PloS One, 2023;18(3):e0281683 https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0281683
16. FDA Approves First Treatment for COVID-19. FDA News Release. U.S. Food and Drug Administration. October 22, 2020. Accessed March 25, 2024. https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-covid-19
17. Coronavirus (COVID-19) Update: FDA Authorizes Monoclonal Antibody for Treatment of COVID-19. FDA News Release. U.S. Food and Drug Administration. November 9, 2020. Accessed April 21, 2024. https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-monoclonal-antibody-treatment-covid-19
18. FDA Takes Key Action in Fight Against COVID-19 By Issuing Emergency Use Authorization for First COVID-19 Vaccine. FDA News Release. U.S. Food and Drug Administration. December 11, 2020. Accessed April 21, 2024. https://www.fda.gov/news-events/press-announcements/fda-takes-key-action-fight-against-covid-19-issuing-emergency-use-authorization-first-covid-19
19. Coronavirus (COVID-19) Update: FDA Authorizes Monoclonal Antibodies for Treatment of COVID-19. FDA News Release. U.S. Food and Drug Administration. November 21, 2020. Accessed April 21, 2024. https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-monoclonal-antibody-treatment-covid-19
20. Tolles J, Luong T. Modeling epidemics with compartmental models. JAMA, 2020;323(24):2515-2516 https://jamanetwork.com/journals/jama/fullarticle/2766672

21. Holmdahl I, Buckee C. Wrong but useful—what covid-19 epidemiologic models can and cannot tell us. New England Journal of Medicine, 2020;383(4):303-305 https://www.nejm.org/doi/full/10.1056/NEJMp2016822
22. Atkeson A. Covid's lessons for future modeling of pandemics. NBER Reporter, 2021;(1):10-15 https://www.econstor.eu/bitstream/10419/265457/1/2021number1-10-15.pdf
23. Saez M, Tobias A, Varga D, Barceló MA. Effectiveness of the measures to flatten the epidemic curve of COVID-19. The case of Spain. Science of the Total Environment, 2020;727:138761 https://www.sciencedirect.com/science/article/pii/S0048969720322786?casa_token=135MLnrPG2QAAAAA:Q-jrfwYkbiI1_bJbfq5-hpmphQ9CASAxnER6pwHe9A-I1DsGMV-jcUL7vT72djwKVUIXbvERN39g
24. Allcott H, Boxell L, Conway JC, et al. What explains temporal and geographic variation in the early US coronavirus pandemic? (No. w27965). Cambridge, Massachusetts: National Bureau of Economic Research, 2020. Accessed April 21, 2024. https://www.nber.org/system/files/working_papers/w27965/w27965.pdf
25. Do TD, Gui MM, Ng KY. Assessing the effects of time-dependent restrictions and control actions to flatten the curve of COVID-19 in Kazakhstan. PeerJ, 2021;9:e10806 https://peerj.com/articles/10806/
26. Wieland T. Flatten the curve! modeling SARS-CoV-2/COVID-19 growth in Germany at the county level. medRxiv, 2020;05 https://www.medrxiv.org/content/medrxiv/early/2020/10/20/2020.05.14.20101667.full.pdf

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COMPILED BY
ROSEANN GIORGIANNI,
DEPUTY STATE REGISTRAR

Rhode Island Monthly Vital Statistics Report
Provisional Occurrence Data from the Division of Vital Records

VITAL EVENTS	REPORTING PERIOD		
	SEPTEMBER 2023	12 MONTHS ENDING WITH SEPTEMBER 2023	
	Number	Number	Rates
Live Births	850	10,867	10.3*
Deaths	885	10,902	10.3*
Infant Deaths	2	47	4.3#
Neonatal Deaths	2	29	2.7#
Marriages	1021	6,668	6.3*
Divorces	218	2,567	2.4*

* Rates per 1,000 estimated population
# Rates per 1,000 live births

Underlying Cause of Death Category	REPORTING PERIOD			
	MARCH 2023	12 MONTHS ENDING WITH MARCH 2023		
	Number (a)	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	192	2,380	216.9	3,105.0
Malignant Neoplasms	194	2,206	201.0	4,674.0
Cerebrovascular Disease	55	512	46.7	614.5
Injuries (Accident/Suicide/Homicide)	84	1,073	97.8	13,872.5
COPD	37	457	41.6	392.5

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.
(b) Rates per 100,000 estimated population of 1,097,379 for 2020 (www.census.gov)
(c) Years of Potential Life Lost (YPLL).

NOTE: Totals represent vital events, which occurred in Rhode Island for the reporting periods listed above.
Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.

RIMS gratefully acknowledges the practices who participate in our discounted Group Membership Program

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Medical Infomercials

JOSEPH H. FRIEDMAN, MD

Recently I've become aware of the increasing use of academic reports to promote sales in the form of infomercials published as research. This isn't a new development, but seems to have become more common. Their frequency is nearing that red line at which "something must be done." Drug companies must do research and must publish their results. Obviously, a drug needs to be proven both safe and effective before it can be approved by the Food and Drug Administration (FDA), and its effects need to be understood by those of us who may prescribe it. In the best of all worlds, we'd also like to see a new intervention compared to old ones, but that's a rare event, since the risk of a new, more expensive drug being found to not be better than an old generic would be a killer event. One can't put Humpty Dumpty back together again.

Most of us, when we consider drug studies, think about the clinical trials that led to FDA approval, or the basic research studies that preceded the clinical trials. However, new drugs are often the subject of "real-life" reports. "Real-life studies" are to be distinguished from research protocol studies. Although there has been much made of "evidence-based medicine," there really aren't appropriate evidence bases for most medical decisions. Data for most studies have stringent inclusion and exclusion criteria which "real-life" patients often don't meet. A "real" patient is 83 and the studies showing drug efficacy excluded patients over 80. The "real-life" patient takes an anti-platelet drug, which was prohibited in a study of anticoagulants. And on and on.

These biased studies are usually sponsored in some way by the drug companies. In some they hire a professional writer, and have a group of known "key opinion leaders," or, "KOLs," as they are known in the trade, paid to meet at a conference, who then later read the manuscript, contribute a critique, and are then considered co-authors.

There are good reasons for these types of studies. I have published retrospective studies of medications used in Parkinson's disease in my own patients. How effective was the drug? How well tolerated was it? I may do this because I have found the drug to be more or less effective, worse or better tolerated than commonly thought, or more flexible in its use than approved by the FDA, which must adhere strictly to the experimental protocol. If a drug was tested only on people under age 65, it can be recommended only for those people, but an individual doctor, or clinic, can report on its findings in people of all ages. Some drug companies will fund such a venture, but most of these studies are not subsidized. I do these studies because I think the contribution may help guide treatment decisions, and, like most academics, I like to see my name in print. I do not do this for money. But some of these studies *are* funded by drug companies, and therein lies the potential for bias. Please note the word, potential. Not all such studies are biased.

I recently reviewed a handful of papers showing that a particular drug, still with patent protection, has a better safety profile than its competitor drug. The methodology was quite reasonable, but, like most methodologies, subject to question. One can usually quibble as to how to categorize responses as mild, moderate or severe, or what is "clinically meaningful," or what constitutes a positive response, or what scale to use to use when 10 different ones to measure the same thing are available. These are unavoidable issues for which there will be differences of opinion. However, a good paper will specifically point out the potential drawbacks of a study, such as the limited study population, the number of subjects being less than would be ideal, the age variation, the concomitant disease prevalence, and so on. However, the papers I thought biased only mentioned the possible flaws in reports

that showed the drug in a less positive light. The supportive studies were not criticized.

These biased studies are usually sponsored in some way by the drug companies. In some they hire a professional writer, and have a group of known "key opinion leaders," or, "KOLs," as they are known in the trade, paid to meet at a conference, who then later read the manuscript, contribute a critique, and are then considered co-authors. These KOL authors lend gravitas and presumed legitimacy to the report, but all have some financial ties to the company, including the meeting they were paid to attend as scientific advisors. These are all noted in the conflict of interest statement that accompanies each article, and all maintain that they participated in the writing of the manuscript by claiming editorial participation, meaning that they read the article, although perhaps not so carefully, and may have contributed meaningful criticisms.

On the other hand, I recently was asked to review another industry-sponsored study that concluded that the study drug was not superior to the comparator generics. I was very happy to see an industry-sponsored study not endorse its drug, although disappointed that the drug wasn't better. The positive aspect was that patients could save money by buying the generic. I don't know how often this occurs. I do not think that companies practice a "catch-and-kill" ethos that pulp newspapers do, but companies try to shy away from explorations that will not likely show their product in a light that will help them sell a product. They favor the much less expensive review of large databases or the personal experience of a physician who endorses their product. I have no idea if they do exploratory forays into the data to get a good idea of the answer before they ask the question. My own motto has been, "never do a drug study that you don't know the result."

Choosing peer reviewers who can recognize bias and maintain an absolute policy of rejecting biased reporting is the best approach to curbing this problem. As far as I'm aware, no article I've recommended rejection due to bias has been accepted by the journal I've reviewed for. The authors will have received an anonymous critique from this peer reviewer recommending that after they revise their paper to submit elsewhere, they have an unbiased reader review their paper as they are apparently unable to recognize their own bias. I am hopeful that each of the authors will have learned a lesson, as an accusation of bias is as scorching a criticism as most researchers ever will get. I am optimistic that such rejections will chasten them forever. ❖

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RIMJ Covers Capture Mid-Century Medical Landscape

MARY KORR
RIMJ MANAGING EDITOR

The covers of the *Rhode Island Medical Journal* (RIMJ) offer a portrait of the state's medical history and innovations, as well as other glimpses of life at the time. Perusing the archives,[1] you never know what you will find, as these covers, captions, and related content from 1974 illustrate.

Weather-wise, looks like some snow decorated the region during the holiday season (**Figure 1**). The March 1974 cover showcased up-to-date modalities in nuclear medicine (**Figure 2**). And, welcoming springtime, the May cover featured the latest post office stamp, (18-cents!), of the first woman physician to receive a medical degree in America, Dr. Elizabeth Blackwell. The caption stated there are many physician philatelists, some of whom specialize in stamps concerning medical subjects (**Figure 3**).

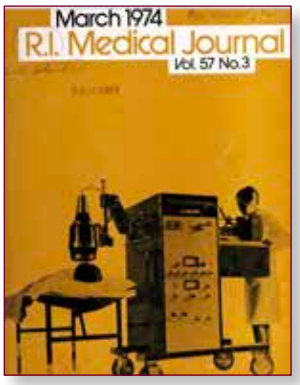


Figure 2. March 1974
Single probe rectilinear scanner illustrated an introduction to nuclear medicine and imaging modalities in use.

V.A. Hospital at Davis Park

The cover and editorial in the June issue 50 years ago showcased the 25th anniversary of the Providence V.A. Hospital at Davis Point (**Figure 4**) (See **sidebar**). According to a 2018 document in the National Register of Historic Places, "State-of-the-art facilities with buildings for research and patient care were the hallmarks of the post-World War II Veterans Administration medical centers, referred to today as the 'third generation' of veterans' hospitals."[2]

Figure 4. June 1974
The Providence V.A. Hospital at Davis Park, which marked the 25th anniversary of its opening on June 6th.

At that time the VA had the largest network of hospitals in the nation. **Figure 5** shows a photo of the main building of the Providence VA

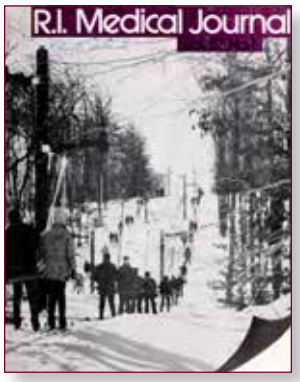


Figure 1. January 1974
Snow makes brief return to Rhode Island ski areas.
[COURTESY OF RHODE ISLAND DEVELOPMENT COUNCIL]

Figure 3. May 1974
Reproduction of postage stamp with image of Dr. Elizabeth Blackwell, first woman physician to receive a medical degree in America.

Figure 5. Providence V.A. Hospital, 1948.
[NATIONAL REGISTER OF HISTORIC PLACES[1]]

The V.A. Hospital at Davis Park[3]

Our cover this month is devoted to the Veterans Administration Hospital of Providence, Rhode Island, located on a commanding hill-top in Davis Park. On June 6th is celebrated the twenty-fifth anniversary of its opening.

The caliber of V.A. medicine can be measured by the stature of the medical authorities who appeared on the anniversary program – all affiliated with V.A. hospitals. One of the more prestigious names was that of **Dr. Rosalyn S. Yalow**, who, with the late **Solomon A. Berson**, developed radio-immunoassay while working in a V.A. hospital.

In the past quarter century, it has served the veterans of Rhode Island well. In the absence of a medical school in the local area, it has been affiliated with Boston University, training residents in both medicine and surgery.

Two new developments were announced in connection with the anniversary celebration. The first is expected approval for the building of an extensive, new, two-story ambulatory wing to provide for a rapidly expanding ambulatory service.

The second development is the formal affiliation in the Brown University Medical School to commence with the coming academic year. The hospital will receive students from the medical school and train residents in the various specialties in coordination with the other teaching hospitals in the Brown system.

We congratulate "The V.A." on the occasion of its observance of twenty-five years of service to the state and its vet-erans and look forward to a continued complete relationship and a closer integration with the medical community of Rhode Island.

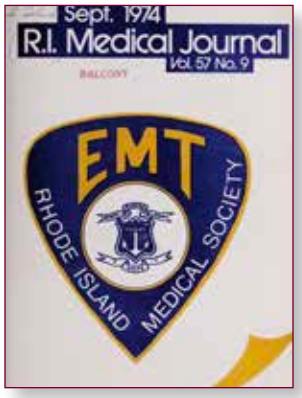


Figure 6. September 1974
The issue described the start of statewide training programs in Emergency Medical Services.

in 1948, one of six of 46 hospitals completed by 1950 to serve the veterans of World War ll.[2]

Emergency Medical Services

The Sept. 1974 issue contained an article by Edward J. Lynch, an RIMJ editor, with photos on the development of formal training courses for the emergency medical services (EMS) in the state (**Figure 6**). The first educational forum was held at The Miriam Hospital in 1970, coordinated by **DR. ROBERT L. CONRAD**, a surgeon and chairman of the Rhode Island Medical Society's Emergency Medical Services Committee, formerly known as the Disaster Committee, and physician members, as well as "rescue squad workers and allied health personnel in their areas of expertise."[3]

The program quickly spread to Newport, Kent, Woonsocket, Fogarty and Memorial hospitals, and statewide ambulance corps. Topics included: vital signs and their significance, medical emergencies, neurological problems, surgical injuries, fractures, the emotionally disturbed and unruly, emergency childbirth, infectious and contagious diseases, environmental emergencies, and car crashes (**Figure 7**).[3]

Figure 7. An EMS training exercise in the early 1970s in Rhode Island on a car accident response. [*RHODE ISLAND MEDICAL JOURNAL*, SEPT. 1974]

The article also described extrication courses. An ice rescue was demonstrated in February 1971 at Roger Williams Park, which proved extremely successful as "practical training exercises." In addition, a curriculum was developed for students at Rhode Island Junio College, which further expanded on the initial EMS statewide training offerings.

In looking ahead, the article noted "the obvious pressure constantly to improve, alter and modify to meet the changing circumstances of the times and the new and expanding frontiers of medical knowledge…even when certification has been achieved for all, there will still be new challenges to be met."

Figure 8: October 1974
"Head of a Child" by Leonardo da Vinci, from the Uffizi Gallery in Florence, Italy. The issue contained a special section on pediatrics.

RIMJ Archives Online

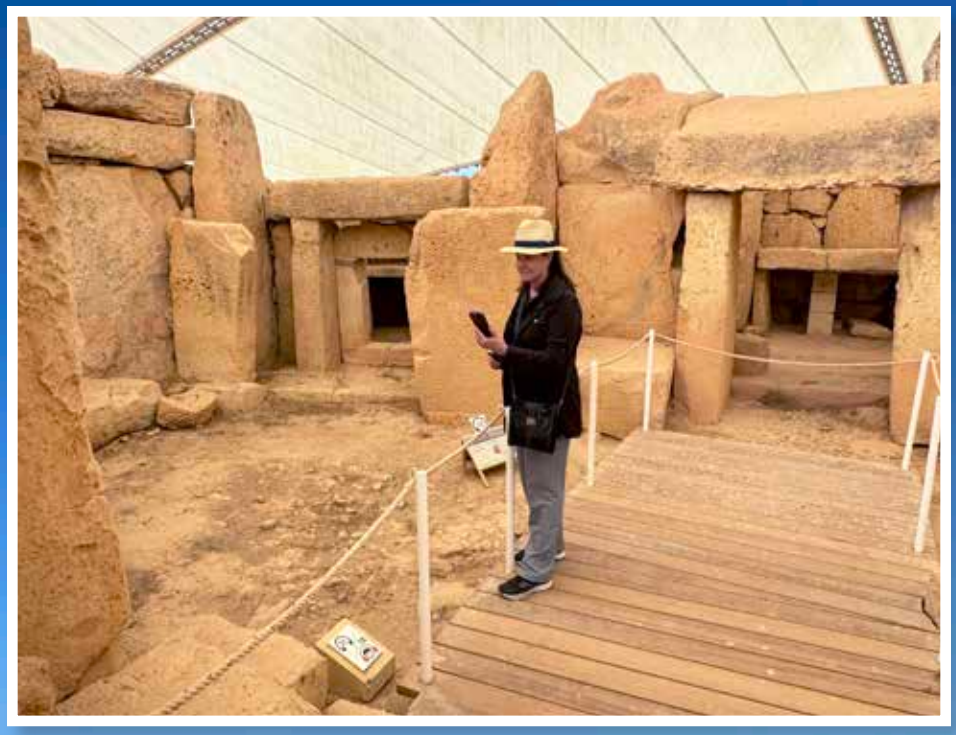
For readers interested in a deeper dive into Rhode Island's medical landscape over the century, archival editions from 1917–2000 can be accessed online.[1] You never know what you will discover – be it a vintage 18-cent-stamp or a Leonard da Vinci illustration in an issue on pediatrics, as shown on the Oct. 1974 cover (**Figure 8**).

References

1. https://guides.library.harvard.edu/c.php?g=947422&p=7661408.
2. https://www.cfm.va.gov/historic/UnitedStates-ThirdGenerationVeteransHospitals-1946-1958-MPSsigned.pdf
3. *Rhode Island Medical Journal*. June 1974; p. 256.

We are read everywhere

In 2024 to date, more than **23,000** unique viewers worldwide have read *Rhode Island Medical Journal* articles or researched topics from its archives, rimedj.org.



MNAJDRA TEMPLE, MALTA

Marianne Migliori, RIMJ Graphic Designer, checks RIMJ within the Mnajdra Archaeological Site. Comprised of huge limestone blocks that were shaped and relocated to the site, it is one of seven megalithic temple sites in Malta, and dates from c. 3500 BCE, making it older than Stonehenge and the Egyptian pyramids. The entire site is now protected by a large architectural canopy.

Mnajdra is located on a rocky cliff overlooking the sea, on Malta's southern coast. About a mile away are a series of caverns accessible only by small boat, collectively known as the Blue Grotto.

The republic of Malta is an archipelago in the Mediterranean Sea, about 100 miles south of Sicily. It covers a mere 122 square miles, with the largest island, Malta, being only 17 miles long and 9 miles wide.

Over the centuries, it has been ruled and influenced by the Phoenicians, Romans, Tunisians, Normans, Turks, French, and British (from 1800–1979). In 1530, the Holy Roman Emperor gave Malta to Knights of Saint John, who built fortifications and the city of Valletta, and who controlled it until 1798 when Napoleon drove them out.

Wherever you may be, or wherever your travels may take you, check the Journal on your mobile device, and send us a photo: **mkorr@rimed.org**.

RI Delegation announces $1.9M to boost RI health infrastructure and workforce

WASHINGTON, DC – Citing the importance of a strong public health infrastructure, including physical and digital infrastructure and a skilled health care workforce, U.S. Senators **JACK REED** and **SHELDON WHITEHOUSE** and Congressmen **SETH MAGAZINER** and **GABE AMO** announced $1,901,154 from the U.S. Department of Health and Human Services (HHS) to support Rhode Island's public health infrastructure. The Rhode Island Department of Health (RIDOH) may use the federal funds to bolster the state's public health workforce, foundational capabilities, technology and data modernization, and physical health infrastructure.

"We're pleased to deliver this federal funding to improve the health and well-being of Rhode Islanders and connect more patients to care, including preventative care," said Reed, Whitehouse, Magaziner, and Amo in a joint statement. "RIDOH and their health partners work hard to keep our communities healthy. This federal funding will help meet critical health infrastructure and workforce needs. It is a smart investment in ensuring the state has the systems, services, and staffing it needs to protect and promote public health."

The federal funding is made available through HHS's Centers for Disease Control and Prevention's (CDC) Strengthening U.S. Public Health Infrastructure, Workforce, and Data Systems grant is a multi-year, multi-billion-dollar investment that supports critical public health infrastructure and workforce needs of jurisdictions across the United States: https://www.cdc.gov/infrastructure/ ❖

BCBSRI's $26M operating loss reflects nationwide trend of increasing healthcare costs

PROVIDENCE – Blue Cross & Blue Shield of Rhode Island (BCBSRI) reported an operating loss of $26 million in 2023, reflecting a substantial surge in medical and pharmacy claims that resulted in costs growing by $195 million, or 10.5%, over the prior year.

Through administrative cost reductions and the positive performance of the plan's investment portfolio, BCBSRI delivered a net gain of $602,000 on a margin of 0.1% of revenue for the calendar year ending Dec. 31.

"Here in Rhode Island, as well as nationally, healthcare costs are growing rapidly, driven by steep increases in utilization and expanding usage of high-cost pharmaceuticals," said **MARTHA L. WOFFORD**, president and CEO of BCBSRI. "In the midst of these escalating cost pressures, BCBSRI sustained significant operating losses, but managed to break even financially. Even more importantly, we delivered the highest quality service to our members, grew our membership, and worked toward improving the affordability, accessibility, quality, and equity of healthcare in Rhode Island."

Year-over-year claims increase by $195 million

Monthly payments to healthcare providers for the care and treatment of members rose $16 million in 2023 to $152 million per month as healthcare costs grew to consume 89.3% of each premium dollar paid.

Annual claims expenses for hospital-administered drugs, medical and surgical services, imaging, and diagnostics grew by $85 million in 2023 from the previous year. Additionally, pharmaceutical claims grew by $75 million in 2023, led by a 1,300% increase in the commercial market's use of some GLP-1 drugs prescribed for weight loss and diabetes. Concurrently, utilization of high-cost specialty medications for autoimmune diseases jumped 20% amid an expansion of approved conditions treated by these specialty drugs.

Membership retention and growth

BCBSRI's medical enrollment grew by 2.3% in 2023 to now cover more than 431,000 members – approximately 10,000 more than year-end 2022. Additionally, Blue Cross dental experienced a 4.5% increase in enrolled members to reach a total of 159,000 covered individuals.

Additional information on BCBSRI's 2023 financial performance as well as the progress achieved advancing our vision of affordable, accessible, equitable, and high-quality healthcare in Rhode Island will be available through the 2023 Mission Report available on BCBSRI.com. ❖

400,000+ Veterans enrolled in VA healthcare over past 365 days, 30% increase over last year

WASHINGTON, DC – The Department of Veterans Affairs announced that it has enrolled 401,006 Veterans in VA healthcare over the past 365 days – 30% more than the 307,831 it enrolled the previous year. This is the most yearly enrollees in at least the past five years at VA, and nearly a 50% increase over pandemic-level enrollment in 2020.

The number of new enrollees increased in all 50 states year-over-year. The states with the most new enrollees over the past year include Texas (41,287 Veterans), California (33,468) Florida (32,712), Virginia (20,537), North Carolina (17,562), Pennsylvania (16,167), Georgia (15,747), Ohio (12,717), Washington (11,873), Illinois (10,167), Colorado (10,028), Arizona (9,789), Tennessee (9,584), and Michigan (9,294). In Rhode Island, 1,092 Veterans enrolled over the past year, a 38.2% increase.

This historic enrollment has been made possible by the bipartisan PACT Act – signed into law by President Biden as a part of his Unity Agenda for the nation – which allowed VA to expand VA healthcare and benefits to millions of Veterans. VA is also conducting the most aggressive outreach campaign in its history, including hosting over 2,600 events since the passage of the PACT Act, launching a $16+ million advertising campaign, using public service announcements, and – for the first time ever – sending text messages to Veterans encouraging them to enroll in VA healthcare. VA is continuing these aggressive outreach efforts throughout 2024, with more than 550 in-person events already scheduled for this year.

"We want every eligible Veteran to enroll in VA healthcare for one simple reason: Veterans who come to VA are proven to have better health outcomes – and pay less – than Veterans who don't," said VA Secretary **DENIS McDONOUGH**. "That's why we've spent the past year meeting Veterans where they are – hosting thousands of events, sending millions of texts, advertising on every corner, and much more – to get them to come to VA. This aggressive outreach campaign has led more Veterans to enroll in VA care than during any year in at least a decade, and we're not slowing down now."

Under the PACT Act, VA has also upgraded the healthcare priority groups for 693,962 Veterans over the past year – meaning that many of those Veterans are now paying lower copays. Since the PACT Act was passed into law, VA has upgraded the priority groups of more than 746,500 Veterans.

VA recently expanded healthcare eligibility for millions of Veterans nationwide, years earlier than called for by the PACT Act. As of March 5, all Veterans who were exposed to toxins and other hazards while serving in the military and meet certain requirements became eligible to enroll directly in VA healthcare. This means that all Veterans who served in the Vietnam War, the Gulf War, Iraq, Afghanistan, the Global War on Terror, or any other combat zone after 9/11 will be eligible to enroll directly in VA healthcare without first applying for VA benefits. Additionally, Veterans who never deployed but were exposed to toxins or hazards while training or on active duty in the United States will also be eligible to enroll. VA also recently expanded healthcare to all World War II Veterans.

VA is able to serve these new enrollees, in part, due to last year's record hiring in VA's Veterans Health Administration. Last year, VA exceeded hiring goals in the Veterans Health Administration – growing at the fastest rate in 15 years and bringing in more than 61,000 new hires – to prepare for an increase in VA healthcare enrollment among Veterans under the PACT Act. In total, VHA now has more employees than ever before in our history, and VA's retention efforts also led to a 20% decrease in turnover rate among VHA employees from 2022 to 2023.

For more information about VA care, visit VA's healthcare website. For more information about the impact of the PACT Act, visit VA's PACT Act dashboard. ❖

VA Providence unveils Canine Therapy Program to boost Veteran care

Moto and his trainer, Sharon Toner, pose for a photo at VA Providence. [VA PROVIDENCE]

PROVIDENCE – The VA Providence Healthcare has announced the successful launch of its Canine Therapy Program, aimed at enhancing the wellbeing and rehabilitation of Veterans within its care. A recent Meet & Greet session with the therapy dogs was a heartwarming success, witnessing an extraordinary engagement between the Veterans and the canines. The event brought smiles, laughter, and an overall uplift in spirits, particularly noted on the psychiatric unit. According to the unit's social worker, the mood was the highest it had been in recent times, illustrating the immediate positive impact of canine companionship.

Various departments collaborated, including Patient Experience, Volunteer Services, Nursing, Social Work, and Environmental Management Services, to integrate this innovative approach into occupational therapy interventions.

The program is partnered with the Windwalker Humane Coalition in this initiative and connected with "Team Toner," comprising canine handler **SHARON TONER** and her therapy dog, Moto, a standard poodle weighing 85 pounds. Moto is a seasoned professional in delivering comfort and affection, adept at engaging with Veterans who seek his companionship and maintaining a respectful distance from those who prefer to observe.

"Team Toner" collaborates weekly with Haley Gardiner, OTR/L, inpatient occupational therapist, on the psychiatric unit. This partnership is not only aimed at improving Veterans' social functioning and managing stress and anxiety but also at enhancing mood and overall mental health. The hope is to expand the program to other units, further embedding the therapeutic presence of canines within the VA holistic care model for Veterans. ❖

Doctors underutilize next-gen antibiotics to fight resistant infections in U.S. hospitals

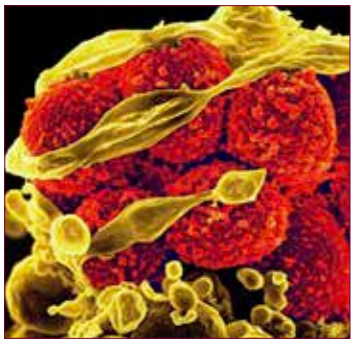
BETHESDA, MD – Despite Food and Drug Administration (FDA)-approval of seven next-generation antibiotics to fight infections caused by resistant "gram-negative" bacteria, clinicians frequently continue to treat antibiotic-resistant infections with older generic antibiotics considered to be less effective and less safe, according to a study by researchers at the National Institutes of Health's (NIH) Clinical Center.

Researchers examined the factors influencing doctors' preference for newer antibiotics over traditional generic agents to shed light on the decision-making processes among clinicians when treating patients with challenging bloodstream infections caused by gram-negative bacteria and significant comorbidities.

The study revealed that at a considerable proportion of hospitals, particularly smaller facilities located in rural areas, staff were reluctant to adopt newer antibiotics. Researchers identified a large cost disparity between older and newer classes of antibiotics; the newer drugs can cost approximately six times more than the older medications, which could disincentivize prescribing.

Researchers also highlight that next-gen agents are prescribed more often at hospitals where lab results that show the medications are effective against a patient's bacterial infection are reported to prescribers. Scientists suggest that earlier and more widespread availability of such lab testing might improve use. Additionally, authors recommend that future public health policies and economic strategies on further development and use of similar antibiotics should be designed to identify and overcome additional barriers.

Gram-negative bacteria are a class of bacteria resistant to multiple drugs and increasingly resistant to most antibiotics. According to the Centers for Disease Control and Prevention, they are able to find new paths of resistant and pass along genetic material that enables other bacteria to become drug resistant.



Scanning electron micrograph of methicillin-resistant Staphylococcus aureus bacteria (red, round items) killing and escaping from a human white blood cell. [NIAID]

This study was funded by the FDA and the NIH Intramural Research Program, by **SAMEER S. KADRI, MD**, *head of the Clinical Epidemiology Section, NIH Clinical Center: Sameer S. Kadri, MD, et al. Assessing Clinician Utilization of Next-Generation Antibiotics Against Resistant Gram-Negative Infections in U.S. Hospitals. Annals of Internal Medicine. April 19, 2024. DOI: 10.7326/M23-2309.* ❖

Bryant introducing Doctor of Clinical Psychology degree


[BRYANT UNIVERSITY]

SMITHFIELD – Bryant University is introducing a Doctor of Clinical Psychology (PsyD) degree, marking the University's first doctoral program. Applications for the new PsyD program open on September 5, 2024, for the first cohort beginning in Fall of 2025.

The new doctoral program is part of Bryant University's School of Health and Behavioral Sciences' commitment to improving healthcare delivery and outcomes, particularly to underserved populations, in Rhode Island, New England, and across the United States.

"We are in the midst of a severe behavioral health crisis, with access to care being a major issue," says **JOSEPH TRUNZO, PhD**, Associate Director of Bryant's School of Health and Behavioral Sciences and clinical psychologist. "The School of Health and Behavioral Sciences at Bryant University is proud to launch this program, training clinicians of the highest quality to help serve the public and alleviate suffering across all populations and settings."

"Bryant University's new Doctor of Clinical Psychology degree demonstrates our growing leadership in the healthcare space," says Bryant University President **ROSS GITTELL, PhD**. "Our strong doctoral program will increase access to mental healthcare for Rhode Islanders by bringing qualified clinicians into the communities where they are most needed."

"Bryant University listens and responds to the needs of our community with high quality, high impact programs," says Bryant University Provost **RUPENDRA PALIWAL, PhD**. "There is an urgent need for qualified clinicians in the mental health field and this new Psy.D. program is key to bolstering the number of clinical psychologists in Rhode Island and across the U.S."

More qualified mental health clinicians needed locally and nationally

The COVID pandemic accelerated a growing mental health crisis across the U.S. There is a growing shortage of qualified, licensed clinical practitioners nationwide and, more specifically, in Rhode Island.

The National Alliance of Mental Illness reports 178,000 adults in RI have a diagnosed mental health condition and 41.5% of adults reported symptoms of anxiety and/or depression. Along with this growing need across the state, there is a mental healthcare desert in Washington and Newport counties, leaving one quarter of a million people without access to care in their own communities. Rising costs are also a factor, with one third of Rhode Islanders who need mental health care unable to access treatment due to cost.

Preparing for clinical careers

The new PsyD degree is built upon the impressive undergraduate psychology program growing at Bryant University's School of Health and Behavioral Sciences, which also offers graduate programs in Physician Assistant Studies and Healthcare Informatics. PsyD students will learn from acclaimed faculty who are leaders in the field and gain valuable experience through a wide range of clinical placements.

Bryant's PsyD curriculum adheres to the scholar-practitioner model of training, which emphasizes clinical practice backed by scientific research. PsyD students will receive a well-rounded education in psychological science and the practice of clinical psychology. Bryant is a leading university in experiential education and PsyD students can expect critical hands-on experience treating patients in clinical settings through practicum placements and a doctoral internship.

PsyD students can opt to specialize in one of two concentrations: Child and Adolescent Psychology and Health Psychology. Both concentrations have a shortage of qualified specialists to provide care to these growing populations.

What will students gain in this program?

In addition to the crucial clinical focus, a Doctoral Research Project is a core part of Bryant's PsyD curriculum. This research will add to the robust work published and presented by the professors in the School of Health and Behavioral Sciences.

The PsyD will also provide exceptional opportunities for Bryant's undergraduate psychology majors to engage and interact with graduate students doing advanced clinical training and research.

Accreditation

Bryant University is accredited by the New England Commission of Higher Education. The Doctoral Program in Clinical Psychology is subject to approval from NECHE.

The American Psychological Association does not allow for application for accreditation until the program has matriculated its second cohort, and it is a multiyear process. The curriculum and the educational experience have been designed and built according to APA accreditation standards. As such, APA accreditation will be pursued at the earliest possible time.

For more information on Bryant's new Doctor of Clinical Psychology program, visit Bryant.edu/Psyd ❖

University Orthopedics partners with Revity Energy

EAST PROVIDENCE – University Orthopedics, the region's largest orthopedic practice, announced today that it is helping to increase the production of clean, sustainable solar energy in Rhode Island through commercial collaboration with Rhode Island-based solar developer Revity Energy.

Revity develops, builds, owns, and operates solar energy generation facilities that feed clean electricity directly to the local utility grid. As part of a virtual net metering program, University Orthopedics' subscription to a shared solar array will help finance the solar energy system. In return for the practice's share of the electricity produced and sent to the grid, Revity will give UOI monthly bill credits.

These reduced energy costs at its Kettle Point location will enable UOI to reallocate funds toward enhancing patient care.

"In addition to providing world-class care, University Orthopedics has always been committed to being a good neighbor and responsible corporate citizen," said University Orthopedics CEO **WEBER SHILL**. "By partnering with Revity Energy, not only are we reducing our own energy costs, we're also reducing our carbon footprint, thus improving community health through lower emissions." ❖

OHIC Public Forum: Rhode Island's National Leadership in Health Care Affordability, Quality & Equity

WARWICK – On Monday, May 13 from 9 a.m. to noon, health care leaders in New England will hold a forum on the latest state and regional health care spending trends and how Rhode Island's efforts to increase affordability compare. Hosted by the Office of the Health Insurance Commissioner (OHIC) and the RI Cost Trends Steering Committee, the forum will feature:

A first look at 2022 statewide performance against Rhode Island's cost growth target:

- New data on health care spending trends
- Public reporting on quality measures at the accountable care organization (ACO) level
- New baseline data on public health and health equity measures

Panel speakers include:

- **DEIDRE GIFFORD, MD, MPH**, Executive Director of Connecticut's Office of Health Strategy
- **CORY KING**, Health Insurance Commissioner, State of Rhode Island
- **DAVID SELTZ**, Executive Director of the Massachusetts Health Policy Commission

The forum will be held at the Crowne Plaza Ballroom, 801 Greenwich Ave., in Warwick. ❖

Southcoast Health Heart and Vascular performs first in New England novel atrial fibrillation treatment

FALL RIVER – Southcoast Health announced the Heart and Vascular program at Charlton Memorial Hospital is the first practice in New England to perform an innovative procedure treating atrial fibrillation (AFib) with the Pulse Select Pulsed Field Ablation (PFA)™ system.

"This accomplishment is a credit to Southcoast Health, our providers and our patients," said **NITESH SOOD, MD**, Director of the Atrial Fibrillation Wellness Program at Southcoast Health Heart and Vascular. "Going from participating in the study for this device three years ago, to performing the first case in New England is a big achievement. This technology offers us the ability to ablate cardiac tissue in areas where, in the past, we were limited with regard to the amount of energy we could deliver. This may help us in treating certain cases."

Led by Dr. Sood, Southcoast Health was the first in New England, 12th in the United States and 16th in the world to complete this procedure.

This new technique features breakthrough ablation technology, pulsed field ablation (PFA) that directs pulsed electric fields to efficiently isolate the pulmonary veins for the treatment of atrial fibrillation.

"It is our goal to be at the forefront of technology and increase the repertoire of what we can offer our patients," said **RAMIN DAVOUDI, MD**, Medical Director of Electrophysiology at Southcoast Health Heart and Vascular. "Our expert team at Charlton Memorial is dedicated to staying up to date with new techniques and technology to ensure we offer our patients a full spectrum of care."

"We're really proud that we were the first in New England to offer this new technology, and this procedure exemplifies that we are a regional leader in all of cardiovascular care," said **PETER COHN, MD**, Physician-in-Chief of Southcoast Health Heart and Vascular. "We are committed to being on the forefront of cardiovascular services, bringing advanced treatment options you would normally only find in large cities to the people in our community." ❖

Boston-Worcester-Providence, MA-RI-NH-CT metro area named 48th in nation for ozone pollution

PROVIDENCE – The Boston-Worcester-Providence, MA-RI-NH-CT metro area was named 48th most polluted in the nation for ozone pollution but third worst in the Northeast region, according to the American Lung Association's 2024 "State of the Air" report, which was released recently.

The Lung Association's 25th annual "State of the Air" report grades exposure to unhealthy levels of ground-level ozone air pollution, annual particle pollution and short-term spikes in particle pollution over a three-year period. This year's report includes air quality data from 2020–2022 and is updated to reflect the new annual particle pollution standard that the U.S. Environmental Protection Agency (EPA) finalized in February.

"In the 25 years that the American Lung Association has been doing our 'State of the Air' report, we have seen incredible improvement in the nation's air quality. Unfortunately, more than 131 million people still live in places with unhealthy levels of air pollution, and the Providence metro area still has work to do," said Daniel Fitzgerald, Director of Advocacy for the American Lung Association. "Climate change is making air pollution more likely to form and more difficult to clean up, so there are actions we can and must take to improve air quality, including policy and practice changes to meet greenhouse gas emission standards set in the 2021 Act on Climate, such as implementing Advanced Clean Cars II and Advanced Clean Trucks rules and calling on EPA to set long-overdue stronger national limits on ozone pollution."

Ground-level Ozone Pollution in the Boston-Worcester-Providence, MA-RI-NH-CT metro area

The "State of the Air" report looked at levels of ozone "smog," the air pollutant affecting the largest number of people in the United States. The Boston-Worcester-Providence, MA-RI-NH-CT metro area ranked 48th worst in the nation for ozone pollution. The ranking was based on the area's worst county's average number of unhealthy days – 3 days per year, a D grade, in Washington County, Rhode Island. This was worse than the area's ranking in last year's report of 52nd worst, with 2.2 days per year, a D grade.

Particle Pollution in the Boston-Worcester-Providence, MA-RI-NH-CT metro area

The report also tracked short-term spikes in particle pollution, which can be extremely dangerous and even deadly. The Boston-Worcester-Providence, MA-RI-NH-CT metro area ranked 101st worst in the nation for short-term particle pollution. The ranking was based on the area's worst county's average number of unhealthy days – 0.8 days per year, a B grade, in Middlesex County, Massachusetts. This was better than the area's ranking in last year's report of 95th worst, with 0.8 days per year, a B grade.

For the year-round average level of particle pollution, the area's worst county, Worcester County, Massachusetts, received a passing grade for pollution levels below the federal standard that was recently updated by the United States Environmental Protection Agency. The Boston-Worcester-Providence,MA-RI-NH-CT metro area ranked 90th worst in the nation. This was worse than the area's ranking in last year's report of 96th worst in the nation.

Findings across Rhode Island

- Washington County earned a D grade for ozone, while Providence and Kent both earned C grades for ozone pollution.
- For short-term particle pollutions, Washington County earned an A grade, with both Providence and Kent earning B grades
- All three measured counties in Rhode Island received passing grades for pollution levels below the federal standard that was recently updated by the United States Environmental Protection Agency.

See the full report results and sign the petition at Lung.org/SOTA. ❖

Senators tour Meals on Wheels, introduce legislation to pilot 'Food as Medicine' interventions

STATE HOUSE – Sens. **VICTORIA GU**, **BRIDGET G. VALVERDE**, **SANDRA CANO**, **ALANA M. DiMARI** , and **JACOB BISSAILLON** toured the headquarters of Meals on Wheels Rhode Island recently to see its work providing essential food support programs to homebound seniors, expecting and postpartum mothers, and other people facing food insecurity. They also discussed how its work relates to legislation to create a Medicaid pilot program to allow medical professionals to prescribe medically tailored meals and "produce by prescription."

"Tackling the root causes of health conditions, whether from poor diet or food insecurity, is an investment that makes sense," said Senator Gu (D-Dist. 38, Westerly, Charlestown, South Kingstown). "Medicaid accounts for about one-third of our state budget. We need to find effective, evidence-based preventative health measures to save on the costs of medical care down the road."

Said Senator Valverde (D-Dist. 35, North Kingstown, East Greenwich, South Kingstown), "Meals on Wheels is already doing great work to address some of the social and nutritional needs of older Rhode Islanders right where they live. I am excited to support passage of this legislation that will allow Meal on Wheels and other agencies to explore expanding the critical work they do into providing evidence-based clinical nutritional solutions to those who might not otherwise be able to afford them."

The legislation (2024-S 2592) sponsored by Senator Gu and cosponsored by Senator Valverde would direct the Executive Office of Health and Human Services to establish a one-year pilot program to provide coverage for evidence-based nutritional assistance for people with clinical needs. This coverage could take the form of produce prescriptions, vouchers or medically-tailored meals, prescribed by medical professionals for persons with diet-related diseases or food insecurity. It could also include clinical nutrition education.

There is a growing evidence base across the country showing that these "food as medicine" programs improve health outcomes and reduce healthcare costs.

The EOHHS would fund the program first with federal dollars through a Medicaid 1115 demonstration waiver, using state funds only if federal funds are unavailable.

From left, Sens. Victoria Gu, Bridget G. Valverde, Sandra Cano, Alana M. DiMario and Jacob Bissaillon and Executive Director of MOWRI Meghan Grady.

"Meals on Wheels of Rhode Island supports Senate Bill 2592 that would authorize the Executive Office of Health and Human Services to establish a program providing coverage for nutritional assistance," said Meghan Grady, executive director of MOWRI. "The bill shows that Senate leaders recognize the contribution that access to healthy food makes to the alleviation and mitigation of hunger, diet-related diseases and health equity."

Meals on Wheels Rhode Island is the state's primary provider of home-delivered meals, delivering 381,049 meals to at-risk individuals in 2023, of which 7,897 were medically tailored meals and 14,215 were culturally responsive meals. ❖

Appointments

RI Representatives join Pediatric and Adult Hydrocephalus Caucus

WASHINGTON, DC – The Hydrocephalus Association announced that Congressman **GABE AMO** (RI-01) and Congressman **SETH MAGAZINER** (RI-02) have joined the Congressional Pediatric and Adult Hydrocephalus Caucus.

Gabe Amo

Seth Magaziner

Congressmen Amo and Magaziner will play an integral role in advocating for increased awareness, funding, and support for pediatric and adult hydrocephalus patients. Their commitment not only amplifies the voice of their constituents who have the condition but also results in heightened advocacy and representation for their needs.

This will allow them to support issues that hit close to home for Rhode Island hydrocephalus patients. Among these constituents is Nikki Batsford, who has been living with hydrocephalus her whole life. Nikki was recently able to share her story with both members of Congress in their district offices.

"We're thrilled to welcome both Congressmen Amo and Magaziner to the Pediatric and Adult Hydrocephalus Caucus," said **DIANA GRAY**, President and CEO, Hydrocephalus Association. "It's fantastic to see both Congressmen joining the Caucus, effectively representing the entire hydrocephalus community in Rhode Island and their need for critical research and improved treatments."

Hydrocephalus affects over 1 million Americans. The only known treatment for hydrocephalus is brain surgery. Anyone at any time can develop the condition from a traumatic brain injury, brain infection, tumor, or, for unknown reasons, as part of the aging process. One in 770 babies develop hydrocephalus each year. Over 800,000 seniors in the U.S. are estimated to have normal pressure hydrocephalus, though the majority are undiagnosed or misdiagnosed as having Alzheimer's or Parkinson's.

"I am excited to join the Hydrocephalus Caucus and work with my colleagues to support research into innovative treatments and a long-term cure," said Congressman Amo. "Thank you to Nikki, a Rhode Islander from Johnston, for working with my office on this issue. I look forward to raising awareness of Hydrocephalus and working to support the over 1 million Americans living with the condition."

"One million Americans live with hydrocephalus, and Congress must work together to help those facing this life-threatening condition," said Rep. Magaziner. "I'm joining the Congressional Hydrocephalus Caucus to support research and advocate for Rhode Islanders and people across the country living with this condition."

The Caucus serves to inform the congressional community about the needs of those living with hydrocephalus, their families, and caregivers. This includes funding for research from the National Institutes of Health and Department of Defense and other key health policy priorities impacting the community such as Medicare and Medicaid access, special education, and rehabilitation services. ❖

Clark Chen, MD, named Director of the Brain Tumor Program

PROVIDENCE – The Norman Prince Neurosciences Institute and the Lifespan Cancer Institute announced the addition of **CLARK CHEN, MD, PhD**, as the Director of the Brain Tumor Program.

Dr. Chen earned a medical degree and doctoral degree in genetics, both from Harvard Medical School. He completed a clinical fellowship in stereotactic neurosurgery at Beth Israel Deaconess Medical Center and clinical fellowship in radiosurgery at Massachusetts General Hospital. His earlier neurosurgical training included the completion of an internship in surgery and residency in neurosurgery, also at Massachusetts General Hospital, with a post-doctoral fellowship at Dana Farber Cancer Institute.

In his nearly two decades of neurosurgery practice in prominent academic institutions, Dr. Chen rose through the ranks and chaired the Department of Neurosurgery at the University of Minnesota before joining Lifespan. In his new role, Dr. Chen will serve as the Director of the Brain Tumor Program within the Department of Neurosurgery at the Alpert Medical School as well as the Co-Director of the Stereotactic Radiosurgery Program. Dr. Chen is an NIH RO1-funded investigator whose research focuses on developing novel diagnostic and therapeutic approaches for brain tumor patients through DNA repair modulation and gene therapy.

Dr. Chen has published over 300 peer-reviewed manuscripts and is consistently recognized with awards, honors, and prizes by national and international organizations for his outstanding administrative leadership, innovative clinical care, and research excellence. ❖

Appointments

Cory King confirmed as Rhode Island Health Insurance Commissioner

PROVIDENCE – **CORY KING** is now the permanent head of Rhode Island's Office of the Health Insurance Commissioner (OHIC), the Rhode Island Senate confirmed in a vote in early April. He has been serving as acting commissioner since December 2022.

He was nominated to the permanent post by Gov. **DAN McKEE** on March 21. Before stepping up to fill the role of acting commissioner, King served as OHIC's Chief of Staff from 2021 to 2022 and also as Director of Policy from 2019 to 2021.

"Cory has proven to be a dedicated, highly capable leader who is committed to fighting every day to improve our state's health care system," said Governor Dan McKee "I'm thrilled to have Cory continue his work to ensure equitable access and comprehensive coverage for all Rhode Islanders.»

During his time at OHIC, King was a key figure in implementing the McKee Administration's Health Spending Accountability and Transparency Program, which gives the state the ability to collect and analyze data on health care spending and quality to promote more affordable health insurance premiums for working Rhode Islanders.

King also helped launch OHIC's Data Hub [zk8ngbyab.cc.rs6.net], which gives the public analytic dashboards on health care spending, utilization, and payment. Additionally, he led the first comprehensive review of Medicaid reimbursement rates for behavioral health services, home and community-based services, and early intervention which resulted in recommendations by the McKee Administration to increase rates.

King completed his undergraduate degree at Tulane University before earning a master's degree in public policy from Brown University in 2013. He is an active member of the Coverage, Cost, and Value Steering Committee for the National Academy for State Health Policy.

"It is an honor to be nominated by Governor McKee to serve as Rhode Island's Health Insurance Commissioner," said King. "I look forward to working in collaboration with all stakeholders to improve Rhode Island's health care system." ❖

Recognition

CODAC's Linda E. Hurley honored with National Council's Lifetime Achievement Award

CRANSTON – The National Council for Mental Wellbeing presented **LINDA E. HURLEY, BA, MA, CAGS**, with its Lifetime Achievement Award in recognition of her distinguished career. The award recognizes individuals for their tireless efforts to improve the lives of those living with mental health and substance use challenges.

Hurley is the president and CEO of CODAC Behavioral Health Care, Rhode Island's oldest, largest and only nonprofit outpatient opioid treatment program. Under Hurley's leadership, CODAC has been a national leader in developing new paradigms for the treatment of opioid use disorder, including creating a national model for medication-assisted treatment services in carceral settings and deploying the first mobile unit to offer methadone services under the new DEA regulations.

Hurley is one of five National Council members who will be honored. The National Council will present two members with a Lifetime Achievement Award and two members with a Peer Specialist of the Year Award. One member will receive the inaugural National Council Legacy Award. All five recipients of the National Council's Awards of Excellence were honored during NatCon24 in St. Louis, Missouri, held April 15–17.

National Council President and CEO Chuck Ingoglia presented Hurley with the award.

"Linda Hurley is a trailblazer and a leader," Ingoglia said. "People in Rhode Island are better off because of her thoughtful leadership. The changes she has introduced have improved substance use treatment and care, and so many people have benefited as a result. She truly is a lifesaver."

In learning of the award, Hurley stated: "I am thrilled and honored to receive this prestigious national award, particularly at this time when CODAC is preparing to launch one of the most fully integrated health and wellness facilities in the country – a place where opioid treatment services will be offered under one roof with primary care, mental health services, dental care, and an onsite, full-service pharmacy. With the addition of a peer recovery community center and essential social services, CODAC will be able to deliver the full spectrum of health services needed by people suffering from addiction." ❖

Recognition

Seth F. Berkley, MD, to receive the 2024 Jimmy and Rosalynn Carter Humanitarian Award

PROVIDENCE – **SETH F. BERKLEY, MD**, senior adviser at the Pandemic Center of Brown University, will receive the 2024 Jimmy and Rosalynn Carter Humanitarian Award in recognition of his work as an innovative entrepreneur, a pioneer in global health, and a champion of equitable access to vaccines.

The National Foundation for Infectious Diseases (NFID) created the award to honor individuals whose outstanding humanitarian efforts and achievements have contributed significantly to improving global public health.

An infectious disease epidemiologist, Dr. Berkley led Gavi, the Vaccine Alliance for 12 years, raising $33.3 billion and increasing coverage of routine immunization in lower-income countries. Gavi has vaccinated more than 1 billion children and introduced more than 600 new vaccines, reducing vaccine-preventable child deaths by 70%, and preventing more than 19.9 million deaths. While at Gavi, he co-created COVAX, a global multilateral solution that worked with partners and leaders of 193 economies to secure, ship, and help deliver nearly 2 billion doses of COVID-19 vaccine to 146 economies. He previously founded the International AIDS Vaccine Initiative (IAVI) to develop an AIDS vaccine for developing countries.

"Seth Berkley restlessly takes on and delivers on big challenges," said **BRUCE G. GELLIN, MD, MPH**, of The Rockefeller Foundation in nominating Dr. Berkley. "Turning vaccines into vaccinations among the most vulnerable and ensuring that routine immunizations were indeed routine, he also played a pivotal role in changing the way the world prevents and responds to global health crises and epidemics."

The award will be presented at the 2024 NFID Awards Gala in Washington, D.C., in September 2024. ❖

Yul D. Ejnes, MD, honored by American College of Physicians

BOSTON – One of Coastal Medical's founding partners **YUL D. EJNES, MD, MACP**, of Garden City Primary Care, won the Alfred Stengel Memorial Award for Outstanding Service to the American College of Physicians (ACP). He accepted this honor at the ACP's annual Convocation ceremony on April 18th in Boston.

This esteemed award, from the nation's largest medical specialty organization, recognizes internal medicine physicians for their innovative, impactful, and sustained contributions to the field. Dr. Ejnes was selected based on his exceptional work as a Master of the ACP and his dedication to advancing the highest standards of medical education, medical practice, and clinical research.

Throughout his career, Dr. Ejnes has held many distinguished positions, received numerous accolades, and has been widely celebrated as a mentor and role model in the medical community. He is currently a member of Coastal's Governance Committee, Immediate Past Chair of the Board of Directors of the American Board of Internal Medicine, and a Clinical Professor of Medicine at Brown Medical School. ❖

Trust in VA among Veteran patients in VA Providence rises to 93.6%

WASHINGTON, DC – In April the Department of Veterans Affairs announced that Veteran trust in VA Providence Healthcare System has risen to 93.6% – up from 91.7% in 2018 (the first year since VA began conducting this survey). Additionally, nationwide trust in VA outpatient care has increased to 91.8% – up from 85.6% in 2018.

This finding is based on a survey of Veteran patients who received VA health care in the past 90 days. Within one week of using VA services, these Veterans were asked whether they trusted VA for their health care needs across a variety of categories – including scheduling an appointment, health care visits, in-person pharmacy, mail-order pharmacy, labs/imaging, and Veteran safety.

This survey mirrors the findings of recent independent studies. According to Medicare's latest nationwide survey of patients, VA hospitals outperformed non-VA hospitals on all 10 core patient satisfaction metrics – including overall hospital rating, communication with doctors, communication about medication, willingness to recommend the hospital, and more. VA health care has also consistently outperformed non-VA care in peer-reviewed studies, overall quality ratings, and affordability for Veterans.

"We have a great team here at VA Providence," said **LAWRENCE CONNELL**, director, "everyone here puts Veterans first – resulting in outstanding care." ❖

Recognition

Endowment created in memory of UOI Spine Surgeon, Dr. Mark Palumbo

EAST PROVIDENCE – After receiving a commitment of $1.5 million from anonymous donors, University Orthopedics, Inc. announced the creation of an endowment in honor of the extraordinary legacy left by the late Dr. Mark Palumbo.

The Mark Palumbo, MD, Endowment for Spinal Surgery Research and Education will help ensure Dr. Palumbo's passion for medicine, teaching, and research will continue to flourish here in Rhode Island by providing financial support, in perpetuity, toward the clinical and academic mission of the Department of Orthopaedics at the Warren Alpert Medical School of Brown University.

"Dr. Palumbo was not just a colleague; he was my friend and mentor. He dedicated his life to providing his patients with world-class, compassionate care, inspiring the surgeons and residents he taught, and advancing the art of spine surgery through research," said **DR. ALAN DANIELS**, Chief of The Center for Spine Health at University Orthopedics. "It is incredibly rewarding to know that the endeavors of this caring, thoughtful man and skilled surgeon will continue to thrive thanks to the creation of this endowment."

The endowment will support both translational research efforts by our staff and the educational initiatives of the University Orthopedic Spine Division.

"These funds will help identify new models of care delivery, building on the significant basic science advances championed by Dr. Palumbo, and ultimately influencing orthopedic innovations at the regional, national, and international level that improve the quality and outcomes of patient care," said Dr. Daniels, who also serves as Chief of Brown University's Orthopedic Spine Division.

Examples of activities impacting clinical outcomes include the development of:

- Novel clinical care models focused on optimizing patient safety and decreasing complications
- Innovative patient applications of new (and existing) technology
- Pioneering surgical procedures in the field of adult and pediatric spine surgery ❖

Kent receives Silver-Level 2 Geriatric Emergency Department Accreditation

WARWICK – Kent Hospital has received the Silver-Level 2 Geriatric Emergency Department Accreditation (GEDA) from the American College of Emergency Physicians for its dedication to providing quality emergency care for older adults. As the only Silver-Level 2 Geriatric Emergency Department in Rhode Island, Kent Hospital joins an exclusive group of less than 100 hospitals nationally to earn the prestigious designation.

The accreditation program was developed to ensure geriatric patients receive well-coordinated, high-quality care during the Emergency Department experience. Silver-Level 2 emergency departments, such as Kent Hospital, have demonstrated specific initiatives that elevate the level of care for seniors and staff trained and dedicated to implementing the hospital's efforts.

"I am proud of our dedicated team who worked tirelessly to earn this recognition, but more importantly, improve the care of our older adults. We know that growth in the over-65 population, in the next five years and beyond, is going to grow exponentially. Currently, geriatric patients account for 18% of our population with this segment growing 46% by 2050. At Kent Hospital, we have committed ourselves to care for our community presently and in the future. Designations such as this reaffirm our commitment to provide the highest quality care for our older patients," said **PAARI GOPALAKRISHNAN, MD, MBA**, president and COO, Kent Hospital.

"This Silver-Level 2 Geriatric Emergency Department Accreditation builds on the strong commitment we have in caring for our older adults at Kent Hospital. For the last three years, we have operated the Acute Care for Elders (ACE) Inpatient Unit, of which there are only 43 nationally. It's just one specialized program in Kent Hospital's Healthy Aging and Serious Illness service line, meant to diagnose, treat, and manage many of the specific issues that are impacting the health and quality of life of our community's aging population. The average age of the 1,300 patients we discharge annually from this unit is 84-years-old and our quality outcomes are exceptional," Dr. Gopalakrishnan added.

Best practices for geriatric EDs include:

- Ensuring geriatric-focused education and interdisciplinary staffing
- Providing standardized approaches to care that address common geriatric issues
- Ensuring optimal transitions of care from the ED to other settings, such as inpatient, home, community-based care, rehabilitation or long-term care
- Promoting geriatric-focused quality improvement, and enhancements to the physical environment, equipment, and supplies

According to the American College of Emergency Physicians, the proportion of the United States population over 65 years of age is projected to nearly double from 43 million in 2012 to 83 million in 2050. Older adults have unique pre-hospital, ED, and inpatient healthcare needs that deserve specially designed care delivery processes. Older adults are more likely to be admitted to the hospital and to have longer ED lengths-of-stay. ❖

Obituaries

LEO MIREN COK, MD, 95, of Warwick, passed away on April 20, 2024. Born in Trieste, Italy, he was the son of the late Andrej and Milica (Golob) Cok.

At the early age of 16, he joined the Slovenian Partisan (Gregorcic Brigade) fighting guerilla style against the Nazi German forces. After a few months he was captured by them and sent to Dachau Concentration Camp near Munich, Germany. Through unbelievable horrors, including being thrown in a mass grave, he managed to crawl out before bulldozers buried the bodies. He survived using his language skills as a camp interpreter long enough until the American forces liberated the camp on April 29, 1945. He said that his victory over the Nazis was that he was still alive.

It was experiencing all this suffering that Leo Cok in 1947 embarked on the journey to become Dr. Cok. He was a graduate of the University of Zagreb, Yugoslavia, (now Croatia), receiving his Doctorate in Medicine in 1953.

In 1956, at the age of 28, he took the SS America from Calais, France to New York, NY. He completed his residency and specialty in Psychiatry at Northern Westchester Hospital in Mt. Kisco, NY. While there he met another recent immigrant working at the hospital from the Dominican Republic, Gladys Lara, PhD.

In 1957, they moved to Kansas City, Missouri and were shortly thereafter married on March 22, 1958. After less than a year and not liking being so far away from the ocean, he was able to secure a job offer from the "Ocean State", i.e., Rhode Island, where he diligently served as the Director of the Alcohol and Drug Abuse unit at the Eleanor Slater State Hospital.

On November 6, 1970, he had a son, Igor Andrew Cok. His marriage lasted 23 years.

Dr. Cok continued to work as Director of Alcohol and Drug Abuse for the State of Rhode Island until his retirement 32 years later in 1990.

In 1994, he met Adeline Lonardo at the gym, and they remained partners until he passed.

He is survived by his beloved son, Igor Andrew Cok of Warwick, and his sister, Vera Vessel of Trieste, Italy. Dr. Cok was the brother of the late Andro Cok.

In his memory, memorial donations may be made to: Doctors Without Borders, 40 Rector Street, 16th Floor, New York, NY 10006, or UNICEF, 125 Maiden Lane, New York, NY 10038, or the RI Food Bank, 200 Niantic Avenue, Providence, RI 02907. ❖