Impressive research and case studies

2019 submissions show quality research and analysis

More than 30 students, residents and fellows submitted abstracts and case studies to Minnesota Medicine, for possible publication and/or presentation at the Minnesota Medical Association annual conference in September.

The quality of the submissions was, overall, very high, according to reviewers. Minnesota Medicine will publish 13 of the submissions seen as being of exceptional quality. Five are in this issue of the magazine; the remaining eight will be published in the November/December issue and the January/February 2020 issue.

The reviewers looked at each manuscript to determine whether the research or case description was clear and complete, whether the methodology was sound, whether the scientific literature review was sufficient and whether the findings had implications for future research. The reviewer comments were sent to those whose abstracts will be published, so they could respond if any changes were suggested.

We thank our reviewers: Devon Callahan, MD; Siu-Hin Wan, MD; Zeke McKinney, MD, MHI, MPH; and Barbara Yawn, MD. Callahan and Wan are members of the Minnesota Medicine Advisory Board; Yawn, now retired, is a former member. McKinney is chief medical editor of Minnesota Medicine.

Uncommon etiology of chronic pancreatitis—histoplasmosis

BY ALEXA ROBBINS, MD; CADE ARRIES, MD; TETYANA METTLER, MD; MEGAN ROTHENBERGER, MD; AND GREGORY BEILMAN, MD

A 58-year-old woman with a history of diabetes mellitus and hypertension presented with a 10-year history of abdominal pain. The pain was associated with chronic pancreatitis thought to be secondary to familial hypertriglyceridemia and pancreatic divisum. Preoperative CT scan showed calcific pancreatitis with necrosis in the pancreatic tail, calcified splenomegaly and perisplenic lymph nodes (Image 1). Her pain persisted despite multiple pancreatic stents; therefore, she underwent a distal pancreatectomy and splenectomy. The histopathologic examination of the pancreatectomy specimen revealed acute and chronic pancreatitis with focal abscess formation and rare granulomas. Interestingly, her histopathologic examination of the spleen reported hyalinized granulomas (Image 2) and rare fungal organisms suggestive of Histoplasma capsulatum (Images 3-4). Follow up histoplasma urine and blood antigen tests were negative. In retrospect, the splenic and pancreatic calcifications and pulmonary nodules demonstrated on preoperative CT could be reflective of prior disseminated histoplasmosis. Fortunately, this patient remained afebrile throughout her course and had no evidence of active fungal infection after surgery.

Histoplasma capsulatum is a dimorphic fungus endemic throughout the Ohio and Mississippi river valleys of North America. Disseminated histoplasmosis occurs in 1 in 2,000 patients with an acute infection, and is most commonly seen in the gastrointestinal (GI) tract, liver, spleen, and bone marrow. The exact incidence of GI tract histoplasmosis is not known because most
Surface Ki-67 expression on histopathology predicts progression to high-grade dysplasia and esophageal adenocarcinoma in patients with Barrett’s esophagus and low-grade dysplasia

BY UMAR HAYAT, MD; HECTOR MESA, MD; JUSTIN PELTOLA, MD; ANDREW HENN, MD; KEVIN SONG, MD; AMY A. GRAVELY, MA; AASMA SHAUKAT, MD; AND BRIAN J. HANSON, MD

Introduction

Diagnosis and treatment of low-grade dysplasia (LGD) in patients with Barrett’s esophagus (BE) remains challenging. The diagnosis of LGD is difficult and suffers from high intra- and inter-observer variability. As a result, guidelines now recommend that all diagnosis of LGD be confirmed by a second pathologist or a panel of pathologists. Despite confirmation of LGD, almost a third of patients will spontaneously regress. One explanation for this high regression rate is the over-diagnosis of LGD. Correctly identifying patients with LGD with increased risk of progres-
Administration and utilization of POLST among long-term care facilities in Minnesota

BY MAHIMA DEVARAJAN, WALTER JUNGBAUER JR, ALEXA LYON, RYAN MCMAHON, KAYLA MURPHY, RILEY SHEARER, TAYLOR WICKLUND, AND LUCY WITCHELL

Background

Provider Orders for Life-Sustaining Treatment (POLST) forms are used, in addition to advanced directives, to provide orders for medical intervention so that healthcare providers can immediately act on a patient’s wishes. However, awareness of the Minnesota (MN) POLST form among providers and how it is currently utilized has not been extensively studied. Understanding POLST utilization in MN can improve future iterations of the POLST form and utilization practices. This project aims to gain a greater understanding of POLST usage in MN by acquiring data from skilled nursing and assisted living facilities, hospice and home care agencies.

Methods

A survey was administered electronically via the online survey platform Zarca to skilled nursing facility, assisted living, and hospice and home care agency administrators with the help of the Care Providers and Leading Age contact lists. The survey asked quantitative and qualitative questions on POLST utilization by these providers. Our sample size was determined by the survey response rate: n=185 for skilled nursing/assisted living/hospice facilities. The survey remained open for a total of 21 days. The data derived from the survey may be affected by response bias. Organizations that are more familiar with POLST or have strong feelings about the form’s use may be more likely to respond; as a result, our sample may not be representative of all skilled nursing/assisted living/hospice facilities.

Results

Of responding facilities, 57.2% were deemed “Rural” (based upon a classification by the U.S. Office of Management and Budget), with the remaining 42.8% classified as “Urban.” When comparing the type of individual who responded to the survey and their opinion of how well POLST functions to achieve its intended purpose (as outlined by the MMA) it was found that approximately 75% of administrators, nursing staff, and social services responded positively to POLST use in their facility.

Conclusion

Surface Ki-67 expression on immunohistochemistry is a promising marker for the risk of progression in BE patients with LGD. Current guidelines recommend patients with LGD undergo endoscopic eradication therapy or yearly endoscopic surveillance. By identifying those patients with highest risk, this marker may help identify patients with LGD most likely to benefit from endoscopic eradication therapy. MM

Umar Hayat, MD, and Andrew Henn, MD, are fellows in the Department of Gastroenterology, University of Minnesota. Aasma Shaukat, MD, is a professor of medicine in the Department of Gastroenterology, University of Minnesota. Hector Mesa, MD, and Justin Peltola, MD are with the Department of Pathology, Veterans Administration Health Care System, Minneapolis. Kevin Song, MD, is a third-year internal medicine resident, University of Minnesota. Amy A. Gravely, MA, is with the Department of Research, Veterans Administration Health Care System. Brian J. Hanson, MD, is a gastroenterologist, Department of Gastroenterology, University of Minnesota.
Fifty-five percent of respondents reported that they have a POLST "champion" in their facility to advocate for the POLST and 67% reported having a policy regarding the implementation of POLST. Of those that reported the use of a POLST "champion," 84% had also responded positively to POLST being used in their facility. Only 2% of facilities with a "champion" reported patients frequently refusing to fill out the POLST, while 5% of facilities with only a policy reported patients frequently refusing to fill out the form. Forty-one out of a total of 76 responding urban counties (53.9%) and 59 out of a total 107 responding rural counties (55.1%) reported the use of a POLST "champion."

**Conclusion**

The majority of responding facilities employ the POLST form and believe that the form is effective. The facilities that indicated that they appoint a POLST “champion” and/or have a policy regarding POLST corresponded to a lower percentage of patients refusing to complete the POLST form. This suggests that these policies could be beneficial to increasing POLST utilization, especially given that approximately 40% of responding facilities indicated a lack of a POLST champion.

Mahima Devarajan, Walter Jungbauer Jr, Alexa Lyon, Ryan McMahon, Kayla Murphy, Riley Shearer, Taylor Wicklund, and Lucy Witchell are second-year students at the University of Minnesota Medical School.

**REFERENCES**


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**Targeted pharmacologic therapy for KCNQ2 potassium channel-related neonatal encephalopathic epilepsy**

**BY TIMOTHY MARINELLI, DO; LAURA SPELTZ, MD; MAC GARRETT; REBECCA SPELTZ PAIZ, MD; AND SONYA WANG, MD**

**Introduction**

Historically, mutations in KCNQ2-coded Kv7.2 potassium channel have been associated with benign familial neonatal epilepsy. However, recently, a more severe phenotype of early infantile epileptic encephalopathy characterized by intractable seizures, infantile spasms, and severe psychomotor impairment has been appreciated. This rare, autosomal dominant syndrome, which typically presents within the first week after birth, has only been identified in about 100 families worldwide.1 Seizures typically cease after several years of life, but patients experience significant developmental delays and poor neurologic outcomes.2 Although current FDA-approved medications are utilized in seizure prophylaxis, there is a possibility that other agents that directly target the deficient potassium channel could provide long-term neurological benefit.

**Case description**

Our team was involved in the care of a patient who presented in the first week of life with intractable seizures that were preceded by a rhythmic, stereotyped cry, followed by irregular eye movements and tonic posturing associated with apnea. EEG showed a consistent electrographic correlate confirming focal-onset seizures with a tonic semiology. At 2 months of life, the patient was diagnosed with new onset infantile spasms. When the initial imaging and extensive metabolic workup were negative, expedited epilepsy genetic panel was sent. This returned positive for a pathogenic heterozygous mutation at KCNQ2 (variant p.Gly290Asp resulting in a G > A substitution), which has been described in the literature in association with a neonatal epileptic encephalopathy.

**Conclusion**

The KCNQ2 channel was identified in the early 2000s as a promising target for antiepileptic medications, primarily because targeting this channel avoids adverse effects on KCNQ1 (a similar voltage-gated potassium channel present on cardiomyocytes). Interference with that channel can compromise cardiac function and cause arrhythmias. This phenomenon is
Minimally invasive hysterectomy and bariatric surgery to improve endometrial cancer survivorship

BY ANOUSHEH SHAFA, MD; AMANIKA KUMAR, MD; DIOGO TORRES, MD; AND TRAVIS J. MCKENZIE, MD

Surgery is curative for the majority of early-stage endometrioid endometrial cancers (EC). The survivors are at risk of mortality from obesity-related comorbidities unless they have sustained weight loss.

A 54-year-old female with class III obesity, type II diabetes mellitus complicated by neuropathy and retinopathy, hypertension, sleep apnea, and fatty liver disease was diagnosed with grade 1 endometrioid EC. She underwent dual surgery with laparoscopic bariatric surgery and robotic-assisted laparoscopic hysterectomy. The perioperative period was uncomplicated, and final pathology was consistent with a stage IA grade 1 EC. In 12 months, she lost 41.3 kilograms and required less insulin, metformin, and anti-hypertensive medication.

Combined minimally invasive hysterectomy and bariatric surgery is a unique approach to promote sustained weight loss in EC survivors and improve survivorship.

Introduction

Endometrial cancer (EC) is the most common gynecologic malignancy in the United States (US). The majority of EC is endometrioid histology, and strongly associated with obesity. Every increase in 5 body mass index (BMI) units (kg/m²) increases the risk of developing EC by 50%. Additionally, mortality is six times greater for morbidly obese women (BMI ≥ 40 kg/m²) compared to non-obese women (BMI < 25 kg/m²) with EC. Fortunately, most new diagnoses of endometrial cancer are early-stage, low-grade disease with a five-year survival rate greater than 96%. Mortality for EC survivors is significantly more likely to be related to obesity-related comorbidities.

Most patients are unaware of the association between obesity and EC, and do not understand the long-term consequences of obesity. This demonstrates an opportunity to educate patients about this association, and to offer treatment options that target both EC and obesity-related comorbidities. Bariatric surgery has demonstrated a decreased risk of EC occurrence in obese patients. Additionally, bariatric surgery decreases risk of mortality from obesity-related comorbidities including diabetes mellitus and heart disease.

To our knowledge, this is the first report of dual surgery including minimally invasive hysterectomy for treatment of EC and bariatric surgery for treatment of obesity-related comorbidities.

Case

A 54-year-old woman, gravida 2 para 2, with medical history significant for class III obesity with a BMI of 50.0, type II diabetes mellitus and heart disease, was diagnosed with grade 1 endometrioid adenocarcinoma arising in the background of complex hyperplasia with atypia. MRI demonstrated a mass measuring 1.7 x 1.8 x 1.7 cm at the uterine fundus with less than 50% myometrial involvement and absent...
lymphadenopathy. She was referred to gynecologic oncology for further assessment. During this appointment, she shared that she was two weeks into the 12-week pre-bariatric surgery program, which is a multidisciplinary program involving an endocrinologist, nutritionist, and psychologist for patients prior to bariatric surgery. We proposed a dual surgery with a robotic-assisted hysterectomy, bilateral salpingo-oophorectomy (BSO), and bilateral sentinel lymph node biopsies at the same time as the Roux-en-Y gastric bypass surgery. An intrauterine device (IUD) was placed for endometrial protection until surgery. At the three-month follow-up appointment, she had no further vaginal bleeding and she was cleared for bariatric surgery after completion of the 12-week program. She underwent the dual surgery two months later.

Preoperatively, the patient weighed 133.9 kg. Her hemoglobinA1c (HbA1c) was 7.3% and DM medication requirements were metformin 1,000 milligrams (mg) twice daily and insulin 320 units (80 units in the morning, 90 units before lunch, and 170 units before dinner). Her HTN medication requirements were enalapril 40 mg and hydrochlorothiazide 25 mg daily. She underwent minimally invasive dual surgery beginning with laparoscopic Roux-en-Y gastric bypass with a 120 cm Roux limb. The surgery was uncomplicated. Immediately following this procedure, the patient was repositioned for a robotic-assisted laparoscopic hysterectomy and BSO. A mini-laparotomy was made to deliver the uterus, because it could not be delivered vaginally secondary to multiple leiomyomata. Frozen pathology of the surgical specimen confirmed a stage IA grade 1 endometrioid EC measuring 3.2 cm at largest diameter and was negative for lymphovascular space invasion. Indocyanine green was injected but did not map to either sentinel lymph node. Given the frozen pathology report and previous reassuring MRI imaging, lymphadenectomy was not performed. This portion of the surgery was also uncomplicated.

The patient was discharged on post-operative Day 2 on a bariatric diet. Her postoperative progress and management of obesity-related comorbidities were followed every six weeks. Her post-operative progress is outlined in Table 1. At approximately six months after surgery, her HbA1c was 6.9% and she required metformin 500 mg twice daily, insulin glargin 45 units twice daily, and Novolog 5 units for carbohydrate-rich snacks. This is significantly lower than her pre-operative requirements. Additionally, her antihypertensive medications were reduced to enalapril 20 mg daily. She also continued to lose weight at each visit, and at her 12-month follow-up had lost 41.3 kg, which is a 30.8% weight loss. She was also followed by the gynecological oncology department, and there has been no evidence of reoccurrence.

### TABLE 1

<table>
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<th>PRE-OPERATIVE</th>
<th>3 MONTHS</th>
<th>6 MONTHS</th>
<th>12 MONTHS</th>
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<td>Weight, kg (BMI, kg/m²)</td>
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<td>1111.3 (40.4)</td>
<td>104.9 (38.1)</td>
<td>92.6 (33.6)</td>
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<tr>
<td>Percent weight loss (%)</td>
<td>15.4</td>
<td>21.6</td>
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<td>30.8</td>
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<td>Type II Diabetes Mellitus</td>
<td>metformin 1000 mg BID, regular insulin 345 units/day</td>
<td>metformin 1000 mg BID insulin glargin 90 units/day</td>
<td>metformin 500 mg BID insulin glargin 90 units/day</td>
<td>metformin 500 mg BID, insulin glargin 54 units/day</td>
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<td>Hypertension</td>
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<td>enalapril 20mg daily</td>
<td>enalapril 20mg daily</td>
<td>enalapril 20mg daily</td>
</tr>
</tbody>
</table>

**Discussion**

Our patient underwent dual surgery including laparoscopic Roux-en-Y gastric bypass immediately followed by robotic-assisted laparoscopic hysterectomy and bilateral salpingo-oophorectomy. Therefore, she was surgically treated for EC, and is without reoccurrence to date. The bariatric surgery addressed the obesity-related comorbidities. Improvement in health was measured by weight loss as well as decreased medication requirements. She had a sustained 41.3 kg weight loss, with a 30.8% weight reduction 12 months after surgery. She also had decreased requirement of insulin and metformin for treatment of type II diabetes mellitus and decreased requirement of antihypertensive medication for treatment of hypertension. Due to her overall health improvement after the dual surgery, she is at decreased risk of mortality from both EC and obesity-related comorbidities.

Hysterectomy is a surgical cure for most stage IA, grade 1 endometrioid EC, but survivors are still at risk of mortality from obesity-related comorbidities. Unfortunately, nearly half of patients with EC are unable to identify obesity as a risk factor for EC and are unaware of the long-term consequences of their obesity-related comorbidities. Each interaction between a provider and an obese female patient is an opportunity for education about the importance of weight loss either to prevent EC or to improve survivorship. It is critical to take advantage of these teachable moments because EC is the most common gynecologic cancer; over 40% of women in the US are obese, and there over 600,000 EC survivors in the US. Many oncologic organizations, including National Cancer Institute (NCI), National Comprehensive Cancer Network (NCCN), Society of Gynecologic Oncology (SGO), American Society of Clinical Oncology (ASCO), and American Cancer Society (ACS), emphasize weight loss interventions as part of EC survivorship care plans. The patient-provider conversation should address the association between obesity and EC, and risk of obesity-related morbidity and mortality.
By taking advantage of this teachable moment, patients are better informed about the importance of and options available for sustained weight loss. The time of cancer diagnosis can also be an impetus for many patients to take action. While there are many nonsurgical options, bariatric surgery has been associated with more rapid and sustained weight loss compared to nonsurgical methods. Additionally, our patient's improvement in health, which was demonstrated by the decrease in medication requirement for both HTN and DM, supports data that bariatric surgery reduces cardiovascular risk and overall mortality by treating obesity-related comorbidities. Lastly, bariatric surgery decreases the risk of EC occurrence by 60%, there is a dearth of literature on the impact of bariatric surgery on patients who currently have EC, which is a novel aspect of our dual surgery.

Our combined approach demonstrates individualized patient-centered care through the efforts of a multidisciplinary, collaborative team including gynecologic oncology, general surgery specializing in bariatric surgery, endocrinology, and psychology. Additionally, dual surgery increases patient convenience and decreases hospital cost by reducing the need for two separate procedures and hospital stays. Dual surgery with minimally invasive hysterectomy and bariatric surgery in patients with EC allows for safe, patient-centered care that can be offered to a specific group of motivated patients in order to treat EC and improve survivorship.

The authors are all with the Mayo Clinic. Anousheh Shafa, MD, is a resident in obstetrics and gynecology. Amanika Kumar, MD, is a gynecologic oncologist. Diogo Torres, MD, is a fellow in gynecologic oncology. Travis J. McKenzie, MD, is a surgeon in the endocrine subspecialty of the Department of Surgery.

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