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Dictum of Success in Pelvic Exenterative Surgery

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Pelvic exenteration represents the standard of care for patients with locally advanced and recurrent malignancies of the pelvis. Although acceptance has been slow due to the historically high rates of morbidity and mortality reported in the 1940s, recent decades have seen dramatic improvements in outcomes. Advances in chemotherapy, radiotherapy and immunotherapy have shifted treatment paradigms, while surgical techniques have evolved and become more finessed [1]. The trio of success in exenterative surgery, both objectively in terms of survival, and subjectively in terms of quality of life and health economics, is based around ***'one-third selection process, one third decision-making and one-third surgical technique'***.

Selection process, standardisation of referral criteria, improved access to services, better coordination of care and careful assessment of individual patients through a dedicated complex colorectal cancer multidisciplinary team can result in significant benefits to patients requiring pelvic exenteration. Streamlined, standardised and well-communicated management can deliver timely, cost-effective and high-quality care resulting in high rates of complete tumour excision of over 90% and low mortality and morbidity [2].

Decision making developments in advanced pelvic oncology relate to improvements in MRI, navigational technology, the use of radiologically–guided, three-dimensional reconstructions to allow complete extensive resections, and greater adoption of neoadjuvant treatments, including reirradiation, intra operative radiotherapy and total neoadjuvant treatment. There is persistent and substantial variation in treatment decision-making for people presenting with advanced/recurrent pelvic cancer worldwide. Most of the decision-making process, including the recommendation to support or not support advanced pelvic cancer surgery, is based on the experience of individuals and centres, and does not follow a comprehensive evidence-based approach that is well supported by cancer specialists, patients and carers. Treatment decision-making has commonly survival as the solely desired postoperative outcome. There is no evidence on important composite measures, such as survival, morbidity, and quality-of-life outcomes, to inform treatment decision-making. Moreover, the definition of optimal outcomes and the views of cancer specialists, health economists, epidemiologists, health policymakers, patients, and carers on their accepted influence on decision-making are lacking. Therefore, the boundaries of pelvic surgical oncology of the future must try to address unwarranted treatment decision-making variation in patients with advanced or recurrent bowel cancer by developing simple evidence-based surgical information that includes patient choice, physical, nutritional, and psychological information, surgical outcomes, patient-reported outcomes (quality of life), morbidity, treatment costs and survival [3,4].

Surgical technique in achieving the holy grail of an R0 margin is determining not only the resectability of pelvic malignancy, but also the radicality of the surgical approach required. If the disease abuts or involves an organ, that organ should be resected en bloc and not 'shaved' free of tumour. This has led to dramatic improvements in R0

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Key Words: *Pelvic exenteration; locally advanced colorectal cancer; recurrent rectal cancer*

rates in the lateral compartments in the pelvis. Refining techniques continue to facilitate 'higher and wider' resections at the periphery of the pelvis as well. Pelvic Exenterative surgery has undergone dramatic evolution in recent decades from what was a palliative procedure in gynaecologic practice. It now represents the possibility of cure for patients with advanced pelvic malignancy and the standard of care for surgical oncologists. The PelvEx collaborative, the Beyond TME Collaboration, and the IMPACT Initiative have played important roles in providing a forum for surgeons to engage with one another and in facilitating the coordinated collection and pooling of data for what remains a relatively uncommon procedure [5,6].

Adding collaboration, teaching and research opportunities to the '**one-third selection process, one third decision-making and one-third surgical technique' trio** will allow specialist surgeons to practice more precision surgery in dedicated institutions, equipped with state-of-the-art technology providing compassionate care through a clinical approach based on direct personal interaction with patients.

REFERENCES

1. Steffens D, Solomon MJ, Young JM, Koh C, Venchiarutti RL, Lee P, et al. Cohort study of long term survival and quality of life following pelvic exenteration. BJS Open [Internet]. 2018 May;2:328-35. Available from: https://pubmed.ncbi.nlm.nih.gov/30263984/
2. Kontovounisios C, Tan E, Pawa N, Brown G, Tait D, Cunningham D, et al . The selection process can improve the outcome in locally advanced and recurrent colorectal cancer: Activity and results of a dedicated multidisciplinary colorectal cancer centre. Colorectal Dis. 2017 Apr;19(4):331-8.
3. Kok END, van Veen R, Groen HC, Heerink WJ, Hoetjes NJ, van Werkhoven E, et al. Association of image-guided navigation with complete resection rate in patients with locally advanced primary and recurrent rectal cancer: A nonrandomized controlled trial. JAMA Netw Open [Internet]. 2020 Jul;3(7):e208522. Available from: https://pubmed.ncbi.nlm.nih.gov/32639566/
4. Voogt ELK, van Zoggel DMGI, Kusters M, Nieuwenhuijzen MGAP, Bloemen JG, Peulen HMU, et al. Improved outcome for responders after treatment with induction chemotherapy and chemo(re)irradiation for locally recurrent rectal cancer. Ann Surg Oncol. 2020 Sep;27(9):3503-13.
5. Solomon MJ. Redefining the boundaries of advanced pelvic oncology surgery. Br J Surg. 2021 May;108(5):453-5.
6. Shaikh I, Aston W, Hellawell G, Ross D, Littler S, Burling D, et al. Extended lateral pelvic sidewall excision (ELSiE): An approach to optimize complete resection rates in locally advanced or recurrent anorectal cancer involving the pelvic sidewall. Tech Coloproctol. Tech Coloproctol. 2015 Feb;19(2):119-20.

Original Article

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Unusual findings during hernia repair surgery. Our experience

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ABSTRACT

Background: Hernia repair operations are among the commonest surgical interventions. Despite being a deeply studied subject, special attention must be given to the possible unforeseen intraoperative findings, a field with very limited literature.

Material and Methods: In a retrospective study, we gathered all the unusual hernia sac contents encountered, from a total of 1,829 hernia operations that were performed in our institution, during a 14-year period.

Results: In our series, uncommon findings were found in 1.2% of the cases, consisting mainly of the vermiform appendix and the urinary bladder, whose prevalence is 0.53% and 0.50%, respectively.

Conclusions: This percentage, although relatively small, is important and must contribute to the surgeon's awareness, in order to assess the surgical field, minimise complications and perform the proper operation according to the findings.

Key Words: *Hernia; rare hernia contents; unexpected sac findings*

INTRODUCTION

Hernias, as an entity, are one of the most thoroughly studied fields of general surgery partly because of their large incidence (about 1/3 of the population presents groin hernias during lifetime) [1], and also due to the long history of surgical treatment approaches, starting with Bassini's first realistic surgical technique at 1884. Many different operative approaches exist and official recommendations can help but not limit surgeons [4]. Furthermore, hernia sac's content can vary, although there are common findings depending on the region

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A hernia in the inguinal region usually contains the omentum and small intestine [2]. Umbilical hernia may contain preperitoneal fat tissue, omentum, and small intestine or a combination of those so as in ventral and epigastric hernias [3]. Nevertheless, the presence of unusual intraoperative findings still challenges the modern surgeon. We present one of the few large studies focusing on unusual findings and uncommon situations during hernia repair in our institution. Our goal is to contribute to the existing literature with a notable number of cases and help surgeons to acquire a high clinical suspicion in rare hernia sac's contents.

MATERIALS AND METHODS

We performed a case-series study of all patients who were admitted to our surgical department during the period from January 2003 to December 2016. Our Institution is a secondary regional center serving a prefecture with a population of more than 85,000 people.

Our study included all patients over 15 years old who

were operated on any type of hernia, electively or in an urgent/emergent way. Following approval from the Institutional Review Board the patients were identified and their charts were reviewed. Data collected included the patients' demographics, type and location of hernia, reason and mode of admission, preoperative and postoperative diagnosis, case management, type of anesthesia, type of operation performed, postoperative course, complications and mortality.

RESULTS

A total of 1,829 hernia operations were carried out in the study period. All hernia repairs were performed in an open way. The majority of them (71.2%) were inguinal hernia repair (1,303 cases), 1187 elective and 116 urgent. Femoral hernia repair was the case for 43 patients, 28 urgent and 15 electives. Finally, the rest were hernia repair in the abdomen region. Umbilical hernia repair was performed in 244 cases (35 urgent and 209 elective). Ventral hernia was found in 175 patients (31 urgent and 144 elective) and epigastric hernia was the cause of admission in 59 patients (7 urgent and 49 elective) (Table 1).

We excluded patients whose hernia sac's content was omentum or small intestine in the inguinal region and preperitoneal fat tissue, omentum or small intestine in the abdomen region. In our series, uncommon findings were found in 1.2% of the cases (22 patients), consisting mainly of the vermiform appendix and the urinary bladder, whose prevalence is 0.53% and 0.50%, respectively. It is noticed that the majority of uncommon findings during hernia repair surgery, are the urinary bladder and the appendix, together consisting of 68.1% of the cases. It is also found that in our series, the male/female ratio presenting unusual findings leans towards men (3.4), which is lower than that for hernia repair in our institution during the 14 year period, which is 3.58. It is furthermore noticed that the majority of the unusual findings occurred in emergent/urgent operations, on the right side and in groin hernia. Sex, age, mode of admission, hernia location, clinical presentation, hernia sac contents, type of operation and anaesthesia and complications (Clavien-Dindo classification) are summarised in Table 2.

TABLE 1. Demographics of cases during study period.

Type	n	M	F	Urgent	Elective
Inguinal hernia	1303	1191	112	116	1187
Umbilical hernia	244	139	105	35	209
Ventral hernia	175	55	120	31	144
Epigastric hernia	56	27	29	7	49
Femoral hernia	43	15	28	28	15

n=Number of patients M=Male F=Female

DISCUSSION

Hernia repair surgery is among the most frequent operations performed. Although it is a well-documented surgical entity, there is scarce documentation in the literature about the possible unusual intraoperative findings the modern surgeon may encounter [5,6]. To the best of our knowledge, we present the largest case series published in the literature so far.

We have shown that within a 14-year period, there was a 1.2% possibility of encountering uncommon intraoperative findings during hernia repair surgery. Although a relatively small percentage, the surgeon must be vigilant and informed about the possible unforeseen findings, in order to prevent complications, and achieve appropriate and prompt decision making for surgical management. The surgeon has to be able to recognise an atypical surgical field and be aware of the possibility to change the plan for hernia repair (herniorrhaphy instead of mesh hernioplasty, or the necessity to use absorbable or biological mesh) if contamination of the field occurs due to bowel resection, or the presence of inflammation as in cases of appendicitis.

The presence of vermiform appendix in the hernia sac is called Amyand's hernia, after Claudius Amyand, the surgeon who first encountered it, and pioneer surgeon of appendicectomy. In the literature Amyand's hernia prevalence is 1% of the inguinal hernias, while in more modern studies, this percentage drops around 0.4-0.6% [9,11], in accordance to our research, where Amyand's hernia prevalence was 0.53%. On the contrary, an inflamed appendix was found in 0.38% of our sample, a percentage significantly higher than the 0.1% of the literature [10,11].

Appendicectomy and non-mesh hernia repair, must follow the finding of inflamed appendix, so as to minimise the possibility of infection. Regarding appendicectomy of a healthy looking, incidentally found appendix, there is controversy among authors, where some suggest prophylactic appendicectomy [10], while others reserve appendicectomy for an inflamed appendix [12].

Furthermore, another point of controversy is whether or not a mesh will be used in the repair. Mesh repair is generally not advised when there is an inflamed organ because of possible mesh contamination, therefore suture repair techniques are preferred [9,10]. Other authors have used mesh repair even in cases with inflamed appendix, without complications [11]. Due to the variety of management, Losanov and Basson presented a 4-type classification of Amyand hernias, and their respective

TABLE 2. Data of patients presenting uncommon findings.

P	Sex	Age	Mode of Admission	Hernia Location	Clinical Presentation	Hernia Sac Contents	Operation	Anaesthesia	Complications (Clavien-Dindo)
P1	M	80	Emergent	Right inguinal hernia	Strangulated hernia Haematuria	Bladder	Bladder debridement, suture repair. Mac Vay herniorrhaphy	General	-
P2	M	67	Elective	Left inguinal hernia	Inguinal hernia	Bladder	Lichtenstein hernioplasty	Spinal	-
P3	F	72	Emergent	Umbilical hernia	Strangulated hernia Small Bowel obstruction	Small bowel with a GIST	Small bowel resection and primary anastomosis. Mesh Hernioplasty	General	I
P4	M	83	Emergent	Right inguinal hernia	Strangulated hernia	Gangrenous appendicitis	Bassini herniorrhaphy Right paramedian laparotomy-Appendectomy	General	III
P5	M	69	Emergent	Right recurrent inguinal hernia	Incarcerated hernia Partial small bowel obstruction	Small Bowel and bladder	Lichtenstein hernioplasty	General	-
P6	M	69	Elective	Right inguinal hernia	Inguinal hernia	Bladder	Bassini herniorrhaphy	Spinal	-
P7	M	78	Emergent	Right inguinal hernia	Incarcerated hernia	Appendix	Lichtenstein hernioplasty	Epidural	-
P8	M	95	Emergent	Right inguinal hernia	Strangulated hernia Peritonitis	Perforated appendicitis	Bassini herniorrhaphy Median laparotomy-Appendectomy –Wash out of peritoneal cavity	General	I
P9	M	93	Emergent	Right inguinal hernia	Incarcerated hernia Closed loop large bowel obstruction	Cecum, Sigmoid colon	Lichtenstein hernioplasty	General	I
P10	M	88	Emergent	Right inguinal hernia	Strangulated hernia Bowel obstruction	Cecum (ischaemic) and appendicitis	Bassini herniorrhaphy Median laparotomy-right colectomy	General	III
P11	M	89	Emergent	Left inguinal hernia	Incarcerated hernia. Peritonitis	Sigmoid colon with Hinchey IV diverticulitis	Bassini herniorrhaphy Median laparotomy and Hartmann's procedure	General	I
P12	F	80	Emergent	Right femoral hernia	Strangulated.hernia Peritonitis	Perforated appendicitis	Femoral ring herniorrhaphy. Median Laparotomy-Appendectomy-Wash out of peritoneal cavity	General	I
P13	M	60	Elective	Left inguinal hernia	Inguinal hernia	Bladder	Lichtenstein hernioplasty	Spinal	-
P14	M	59	Elective	Right inguinal hernia	Inguinal hernia	Bladder	Lichtenstein hernioplasty	Spinal	-
P15	M	76	Emergent	Right inguinal hernia	Incarcerated hernia	Appendicitis	Darn herniorrhaphy Median laparotomy-Appendectomy	General	-
P16	M	46	Elective	Right flank incisional hernia	Inguinal hernia	Right liver lobe	Mesh hernioplasty	General	-
P17	F	61	Emergent	Left Spigelian hernia	Strangulated hernia	Sigmoid colon Left ovary and fallopian tube	Left salpingoophorectomy Herniorrhaphy	General	-
P18	M	64	Emergent	Right inguinal hernia	Incarcerated hernia. Haematuria	Bladder diverticula	Lichtenstein hernioplasty	General	-

TABLE 2. Data of patients presenting uncommon findings *(continued)*.

P	Sex	Age	Mode of Admission	Hernia Location	Clinical Presentation	Hernia Sac Contents	Operation	Anaesthesia	Complications (Clavien-Dindo)
P19	F	73	Elective	Incisional hernia (Pfannenstiel incision)	Incisional hernia	Right colon and terminal ileum with adenocarcinoma of the ceacum	Right colectomy and primary anastomosis. Mesh (vicryl) hernioplasty	General	I
P20	F	53	Emergent	Umbilical hernia	Strangulated	Meckel's diverticulum	Small bowel resection and primary anastomosis. Mesh hernioplasty	General	-
P21	M	86	Emergent	Right inguinal hernia	Strangulated	Gangrenous appendicitis	Appendectomy Bassini herniorrhaphy	Spinal	-
P22	M	83	Elective	Bilateral inguinal hernias	Inguinal hernia	Appendix on the right side. Small bowel with neuroendocrine tumor on the left side	Small bowel resection and primary anastomosis. Lichtenstein hernioplasty on the right side and Bassini herniorrhaphy on the left side	Epidural	I

P: Patient, M: Male, F: Female

management [12]. In our series, regarding the cases with an inflamed appendix (type 2), appendicectomy was performed, in one case through hernia, and in the other two through laparotomy in order to secure appendiceal stump because of severe inflammation at the base of the vermiform appendix. The three cases presenting with appendicitis and concurrent peritonitis (type 3), were managed with appendicectomy through laparotomy as indicated. Concerning the two cases with incidentally found macroscopically healthy appendix, reduction to the peritoneal cavity was preferred, followed by mesh hernioplasty (type 1), as indicated.

De Garengeot's hernia, defined as the presence of the appendix in a femoral hernia, has a similar approach to Amyand's hernia. With very limited reports in the literature, a standardised operative pattern does not exist [13]. In our series, only one case with a perforated appendicitis along with peritonitis was encountered, and suture herniorrhaphy with appendicectomy through laparotomy was mandatory to wash out the peritoneal cavity.

The presence of urinary bladder in the sac is reported in the literature between 1 and 4% of all inguinal hernias [6]. In our series, this percentage was 0.5%, significantly lower than that reported in the literature. The presence of bladder diverticula, as in one of our cases, is even scarcer with the literature consisting solely of few case reports [6,8,14]. The surgeon must be aware of the possibility of urinary tract herniation in order to avoid frequent (12%) complications such as bladder injury, while preoperative evaluation such as sonography is advised to selected patients [6]. In case of bladder presence in an incarcerated hernia, where the complication rate is even higher (reported 28.6%), there must be alertness for haematuria, like in our cases, and the use of a Foley catheter must be considered [5].

In female patients, the presence of ovaries and/or fallopian tubes in the hernia sac is encountered in 2.9% of inguinal hernias according to the literature [8]. It is associated with genital tract abnormalities and is more frequently found in the pediatric population [15]. Again, organ salvation must be pursued unless signs of inflammation or strangulation are present [8]. In our case, the left ovary the left ovary and fallopian tube were herniated in a Spigelian hernia, an even scarcer entity with a literature comprising only three case reports [17].

The presence of sigmoid colon in the hernia sac is a rare entity, and follows the same management principles discussed above. In our series, along with two cases of sigmoid colon herniated in a left hernia, we encountered the extremely rare entity of a sigmoid colon herniated in a right inguinal hernia. Only 4 such cases were reported so far [16]. Another rarity is the presence of herniated sigmoid colon with diverticulitis as a content of a left inguinal hernia. It is not clear if the diverticulitis is the result of hernia incarceration or the vice versa. To the best of our knowledge, this is the fourth such case reported so far [18,19]. A Hartmann's procedure, due to perforation, followed by Bassini hernia repair, was performed in our case.

Transabdominal herniation of the liver is another extremely rare entity and only very few case reports

have been published [20,21]. Liver herniation is, in most cases, diaphragmatic and occurs congenitally or after blunt trauma. We presented a right flank incisional hernia containing the right liver lobe, in a non-cirrhotic patient, where mesh repair was used without complications.

In our series of uncommon findings, we must absolutely point out the occurrence of three gastrointestinal tumours as hernia contents. The presence of a small bowel Neuroendocrine Tumour (NET), a small bowel Gastrointestinal Stromal Tumour (GIST), and an adenocarcinoma of the caecum, raises not only hernia management issues, but also oncological ones. Although rare entities with scarce case reports [22-28] they must not be missed, as they thoroughly change the operative plan. In our series both small bowel tumours (NET and GIST) were managed with small bowel resection and primary anastomosis, followed by hernia repair, while in the case with the adenocarcinoma of the caecum, right colectomy and primary anastomosis followed by absorbable mesh hernioplasty was performed. One case presented as an emergency.

A Littre's hernia is a very rare hernia, which is defined by the presence of Meckel's diverticulum in a hernia sac. Its frequency as an umbilical hernia is estimated to be 11.3% and it occurs mainly in female patients at mean age of 52 years old, like our patient. Strangulation of a Littre's umbilical hernia occurs in one third of the patients [29].

CONCLUSIONS

Uncommon findings during hernia repair surgery, although rare, pose difficulties to the surgeon, demand vigilance for early detection of their presence, and challenge for appropriate decision making and management upon discovery. The goal of this study is to contribute to the limited literature around the issue, highlighting the need for further documentation, aiming for effective and efficient surgical management.

Ethical standards declaration: *Written consent of the patients.*

Conflict of interest: *None*

REFERENCES

1. Primatesta P, Goldacre MJ. Inguinal hernia repair: Incidence of elective and emergency surgery, readmission and mortality. Int J Epidemiol 1996 Aug;25(4):835-9.
2. Goyal S, Shrivastva M, Verma RK, Goyal S. "Uncommon contents of inguinal hernial sac": A Surgical Dilemma. Indian J Surg. 2015 Dec;77(Suppl 2):305-9.
3. Kulaçoğlu H. Current options in umbilical hernia repair in adult patients. Ulus Cerrahi Derg. 2015 Sep;31(3):157-61.
4. Simons MP, Aufenacker T, Bay-Nielsen M, Bouillot JL, Campanelli G, Conze J, et al. European Hernia Society guidelines on the treatment of inguinal hernia in adult patients. Hernia. 2009 Aug;13(4):343-403.
5. Goyal S, Shrivastva M, Verma RK, Goyal S. Uncommon contents of inguinal hernial sac: A Surgical Dilemma. Indian J Surg. 2015 Dec;77(Suppl 2):305-9.
6. Pirvu C, Pantea S, Popescu A, Grigoras ML, Bratosin F, Valceanu A, et al. Difficulties in diagnosing extraperitoneal ureteroinguinal hernias: A Review of the Literature and Clinical Experience of a Rare Encounter in Acute Surgical Care Settings. Diagnostics (Basel). 2022 Jan;12(2):353.
7. Ballas K, Kontoulis T, Skouras Ch, Triantafyllou A, Symeonidis N, Pavlidis T, et al. Unusual findings in inguinal hernia surgery: Report of 6 rare cases. Hippokratia. 2009 Jul-Sep;13(3):169-71.
8. Gurer A, Ozdogan M, Ozlem N, Yildirim A, Kulacoglu H, Aydin R. Uncommon content in groin hernia sac. Hernia. 2006 Apr;10:152-5.
9. Michalinos A, Moris D, Vernadakis S. Amyand's hernia: A review. Am J Surg. 2014 Jun;207(6): 989-95.
10. Sharma H, Gupta A, Shekhawat NS, Memon B, Memon MA. Amyand's hernia: A report of 18 consecutive patients over a 15-year period. Hernia. 2007 Feb;11(1):31-5.
11. Inan I, Myers PO, Hagen ME, Gonzalez M, Morel P. Amyand's hernia: 10 years' experience. The Surgeon. 2009 Aug;7(4):198-202.
12. Losanoff JE, Basson MD. Amyand hernia: A classification to improve management. Hernia. 2008 Jun;12(3):325-6.
13. Linder S, Linder G, Månsson C. Treatment of de Garengeot's hernia: A meta-analysis. Hernia. 2019 Feb;23(1):131-41.
14. Fuerxer F, Brunner P, Cucchi JM, Mourou MY, Bruneton JN. Inguinal herniation of a bladder diverticulum. Clin Imaging. 2006 Sep-Oct;30(5):354-6.
15. Al Omari W, Hashimi H, Al Bassam MK. Inguinal uterus, fallopian tube, and ovary associated with adult Mayer-Rokitansky-Küster-Hauser syndrome. Fertil Steril. 2011 Mar;95(3):1119.e1-4.
16. Bali C, Tsironis A, Zikos N, Mouselimi M, Katsamakis N. An unusual case of a strangulated right inguinal hernia containing the sigmoid colon. Int J Surg Case Rep. 2011;2(4):53-5.
17. Khadka P, Sharma Dhakal SK. Case report of ovary and fallopian tube as content of a Spigelian hernia - a rare entity. Int J Surg Case Rep. 2017;31:206-8.
18. Arnold N, Ernst AA. Acute sigmoid diverticulitis within a non-incarcerated hernia. Am J Emerg Med. 2015 Jul;33(7):986.e1-2.
19. Tufnell ML, Abraham C. A perforated diverticulum of the sigmoid colon found within a strangulated inguinal hernia. Hernia. 2008 Aug;12(4):421-3.
20. Tekin F, Arslan A, Gunsar F. Herniation of the liver: An extremely rare entity. J Coll Physicians Surg Pak. 2014 Nov;24 Suppl 3:S186-7.
21. Saujani S, Rahman S, Fox B. Budd-Chiari syndrome due to right hepatic lobe herniation: CT image findings of two rare clinical conditions. BJR Case Rep [Internet]. 2017 Mar;3(3):20160133. Available from: https://pubmed.ncbi.nlm.nih.gov/30363244/
22. Goyal A, Mansel RE, Goyal S. Gastrointestinal stromal

tumour in an inguinal hernial sac: An unusual presentation. Postgrad Med J. 2003 Dec;79(938):707-8.
23. Tinoco-González J. Gastrointestinal stromal tumor (GIST) presenting as a groin mass mimicking and incarcerated hernia. Int J Surg Case Rep. 2015;6C:166-8.
24. Christodoulidis G, Perivoliotis K, Diamantis A, Dimas D, Spyridakis M, Tepetes K. An appendiceal carcinoid tumor within an amyand's hernia mimicking an incarcerated inguinal hernia. Case Rep Surg. 2017;2017:5932657.
25. Bacalbasa N, Costin R, Orban C, Iliescu L, Hurjui I, Hurjui M, et al. Incidental finding of a neuroendocrine tumor arising from meckel diverticulum during hernia repair - A Case Report and Literature Review. Anticancer Res. 2016 Apr;36(4):1861-4.
26. Khaled Y Elbanna, Hassan A Alzahrani, Fahad Azzumeea, Hyetham A Alzamel. Neuroendocrine tumor of the appendix inside an incarcerated Amyand's hernia. Int J Surg Case Rep. 2015;14:152-5.
27. Marsden M, Curtis N, McGee S, Bracey E, Branagan G, Sleight S. Intrasaccular caecal adenocarcinoma presenting as enlarging right inguinoscrotal hernia. Int J Surg Case Rep. 2014;5(10):643-5.
28. Meniconi RL, Vennarecci G, Lepiane P, Laurenzi A, Santoro R, Colasanti M, et al. Locally advanced carcinoma of the cecum presenting as a right inguinal hernia: A case report and review of the literature. J Med Case Rep. 2013 Aug;7:206.
29. Schizas D, Katsaros I, Tsapralis D, Moris D, Michalinos A, Tsilimigras DI, et al. Littre's hernia: A systematic review of the literature. Hernia. 2019 Feb;23(1):125-30.

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Optimizing outcomes in symptomatic spinal metastases from non-small cell lung cancer: Evaluating the role of salvage surgical intervention in a multidisciplinary context - A Narrative Review

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ABSTRACT

Background: Lung cancer, a leading cause of cancer-related mortality worldwide, often metastasises to the spine, resulting in significant morbidity and complex treatment challenges. The management of spinal metastatic disease from lung cancer necessitates a multidisciplinary approach, given the array of potential interventions including surgery, radiation therapy, chemotherapy, and supportive care. The selection of appropriate therapeutic strategies is influenced by multiple factors, including disease staging, patient health status, and symptomatology.

Aim: This review article aims to explore the current landscape of surgical intervention for spinal metastases from lung cancer, evaluating its role, efficacy, and the criteria for patient selection within the context of multidisciplinary care. Additionally, it seeks to provide an overview of the existing treatment modalities, highlighting the importance of a tailored approach based on individual patient needs.

Methods: An extensive review of the literature was conducted, focusing on studies, clinical trials, and meta-analyses published on the treatment of spinal metastases in lung cancer patients. Special attention was given to works discussing the surgical outcomes, prognostic factors, and the evolution of treatment protocols over recent decades.

Results: Surgical treatment for spinal metastases from lung cancer is beneficial for select patients, particularly

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those without prior systemic treatments and those in good overall health. The decision to pursue surgery should be made within a multidisciplinary team, taking into account the patient's specific situation and potential to benefit from the intervention. Research advancements and technological innovations continue to refine surgical techniques and improve patient outcomes.

Conclusion: While the role of surgery in treating spinal metastatic disease from lung cancer is limited, it remains a critical option for appropriately selected patients. Future research should aim to further define and expand the criteria for surgical candidacy, enhancing the precision of patient selection and tailoring of treatment strategies. Emphasis on a multidisciplinary approach is essential for optimising outcomes and advancing care for patients with this challenging condition.

KEY WORDS: *Non-small cell lung cancer; small cell lung cancer; spinal metastases; bone metastasis; spinal cord compression; osteolytic metastasis; surgical intervention; multidisciplinary approach*

INTRODUCTION

Lung cancer stands as a predominant cause of mortality attributed to cancer worldwide, with classification into two primary types: small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). A prevalent complication observed in the advanced stages of lung cancer is spinal metastasis, which involves the dissemination of cancer cells from the primary tumour site to the vertebral column. This condition results in significant clinical manifestations, including pain, neurological impairment, and a spectrum of other debilitating symptoms. Lung cancer is identified as the principal origin for approximately 80% of spinal metastases, positioning the skeletal system as the third most common site for cancer metastases, following the liver and lungs. Metastases of the osteolytic type, notably from the lung, kidney, thyroid, and gastrointestinal tract, are particularly concerning [1,2].

Extensive review of relevant literature and clinical observations have established that spinal metastases constitute the most frequent complication among cancer patients, affecting roughly 70% of individuals diagnosed with cancer. Given that lung cancer is the foremost cancer type to metastasise to skeletal structures, it is anticipated that a minimum of 40% of individuals with lung cancer will develop bone metastases throughout their disease trajectory [3]. The emergence of bone metastasis significantly impacts patients' independence, functionality, and quality of life, while also escalating disability, mortality rates, hospitalization costs, and duration of hospital stays [4,5]. Metastatic involvement of the vertebral column is recognised as a distressing condition that adversely affects morbidity, functional disability, and survival expectancy. Reports indicate that nearly half of the individuals succumbing to cancer have vertebral column metastases, with 10% experiencing spinal cord compression [6].

This manuscript aims to explore the clinical scenario of lung cancer metastasizing to the spine and the role of surgical intervention as a palliative measure in select cases. It is critical to underline that the option of surgical treatment remains a subject of debate, and the surgical approach is sometimes viewed with skepticism. This stems from the fact that surgical intervention is not traditionally included within the conservative management spectrum for lung cancer but is considered for cases exhibiting progressive neurological deficits [7].

METHODOLOGY

In conducting this review, a comprehensive literature search was performed across several major databases, including PubMed, Scopus, and Web of Science, to gather relevant information on the surgical management of spinal metastases from non-small cell lung cancer. The search strategy employed a combination of keywords such as "non-small cell lung cancer," "spinal metastasis," "surgical treatment," "multidisciplinary approach," and "patient outcomes." The selection criteria were focused on articles published in English, with a particular emphasis on clinical trials, observational studies, and meta-analyses that discussed outcomes, prognostic factors, and the evolution of surgical and multidisciplinary treatments for spinal metastases in lung cancer patients. This methodological approach enabled the identification and synthesis of critical insights into the current state and future directions of surgical care for spinal metastases from non-small cell lung cancer.

EPIDEMIOLOGY, PATHOPHYSIOLOGY AND DIAGNOSIS

Spinal metastasis represents a common complication in lung cancer, affecting approximately 20-40% of patients

in the advanced stages of the disease. The likelihood of developing spinal metastases escalates as lung cancer progresses, with a higher prevalence observed in individuals diagnosed with NSCLC compared to those with SCLC [3-5]. Approximately 60-70% of SCLC patients will have extensive disease at diagnosis, with a significant portion developing spinal metastases. SCLC's rapid growth and early dissemination patterns contribute to this higher rate of spinal involvement. However, while NSCLC has a lower overall metastatic rate at diagnosis compared to SCLC, the higher prevalence of NSCLC means it also contributes significantly to the number of spinal metastases cases [1-4]. The underlying mechanisms of spinal metastasis in lung cancer are intricate and involve multiple factors. Cancer cells can colonise the spine via hematogenous spread, lymphatic dissemination, or direct invasion of adjacent tissues. This metastatic involvement can lead to spinal cord or nerve root compression, manifesting as pain, neurological deficits, and a range of other clinical symptoms. Furthermore, pathological fractures of the spine due to metastatic lesions significantly contribute to patient morbidity [4,5].

Diagnosing spinal metastases in lung cancer poses considerable challenges and necessitates an integrated approach that includes detailed patient history, physical examination, and diagnostic imaging. Tools such as X-rays, computed tomography (CT) scans, and magnetic resonance imaging (MRI) are pivotal in the assessment and identification of spinal metastases. In certain scenarios, biopsy or the acquisition of tissue samples may be imperative to establish a definitive diagnosis [4-6].

SURGICAL MANAGEMENT OF LUNG CANCER WITH SPINAL INVASION

Lung cancer frequently exhibits growth and intrathoracic spread, alongside metastases to various organs. Predominant metastatic sites include supraclavicular and inferior cervical lymph nodes, liver, brain, bones, and adrenal glands [4,5]. Approximately 40% of patients with lung cancer develop bone metastases, predominantly of the osteolytic type, leading to significant morbidity. This includes pathological fractures, nerve root compression, bone pain, spinal cord compression, neoplastic bone marrow infiltration, and hypercalcemia of malignancy. These complications arise from increased bone metabolism, primarily due to enhanced bone resorption, and are managed through radiation therapy, specific radioisotope administration, surgical intervention, and analgesic treatment [3].

The onset of lung cancer metastases to the vertebral column can occur at any stage of the disease, through direct extension, hematogenous spread, or lymphatic routes. While these tumours are generally considered incurable, advancements in technology have enabled the possibility of radical surgical interventions [2]. Remarkably, 10% of patients with vertebral metastases are unaware of their cancer diagnosis, with spinal cord compression often being the initial presenting symptom; 5% of these cases are due to lung cancer [7]. Lung tumours typically develop osteolytic metastases, demonstrating a tendency for osteotropy. The radiographic appearance of bone metastases varies based on the degree of osteolysis or bone formation, the primary tumour, and its location [9].

The impact of malignancies on the vertebral column includes structural weakness, ataxia, and severe pain, necessitating immediate surgical intervention for stabilization [10]. Primary lung tumours invading the spine can cause excruciating pain and Horner syndrome, with the pain intensifying as the cancer progressively destroys vertebral bodies [2,11].

Following the findings from a randomised trial by Patchell et al. in 2005, the importance of decompressive surgical resection in managing metastatic spinal cord compression has been established [12]. The goal of surgical treatment is to decompress the spinal canal by removing the tumour mass. This is complemented by minimally invasive techniques such as spondylodesis for vertebral column stabilization and spondylosyndesis through various surgical approaches, alongside kyphoplasty and stereotactic radiotherapy. Surgical management of vertebral metastasis is primarily palliative, focusing on spinal canal decompression and stability restoration [13].

Percutaneous vertebral augmentation techniques, like percutaneous kyphoplasty (PKP) and percutaneous vertebroplasty (PVP), offer minimally invasive alternatives for managing painful spinal metastases, especially in high-risk patients [14,15]. Studies by Zhang et al. have shown PKP to significantly correct kyphosis compared to conservative treatments, providing substantial pain relief and functional improvement while preventing further local kyphotic deformation [15]. Direct decompressive surgery followed by postoperative radiotherapy has proven more effective than radiotherapy alone in improving muscle strength, functional capability, and overall survival rates [16].

However, the utility of PKP in a palliative setting does not extend to improving patient survival rates, despite enhancing quality-adjusted life years (QALY) and indicating improved life quality post-treatment [17]. The surgical approach for lung tumours invading the spine and its contribution to cancer therapy remains a topic of debate, with clinical evidence indicating poor survival

rates post-surgical treatment for spinal involvement due to lung cancer [10,17].

It is crucial to evaluate prognostic factors in the decision-making process for treating bone metastases in lung cancer. Tokuhashi et al. proposed six prognostic factors for assessing survival chances in patients with metastatic vertebral column tumours, including (i) the number of vertebral metastases, (ii) the presence of internal organ translocations, (iii) the severity of spinal cord paralysis, (iv) the patient's overall health condition, and (v) the presence of non-vertebral bone metastases [18].

The revised Tokuhashi, Tomita, modified Bauer, and Oswestry scores are frequently utilised as tools for predicting the survival of patients with spinal metastases and assisting in the decision-making process concerning surgical interventions [19-22]. Nevertheless, these prognostic indicators often provide a prognosis for patients with lung cancer that is more pessimistic than warranted. Studies showed that the Tokuhashi scores outperformed the Tomita score; nonetheless, they continued to provide prognostic estimates that were too low for 35% to 40% of the patients [23].

Other prognostic factors, including the number of bone metastases, the primary tumour's malignancy degree, and visceral metastasis to major organs, play a critical role in assessing the feasibility and utility of surgical interventions in the vertebral column [20]. Prognosis remains particularly poor for patients with bone metastases, metastases to vital organs, and direct spinal invasion, especially in cases of superior sulcus tumours [24-27]. Therefore, the decision to proceed with surgical intervention in patients with lung cancer invading the spine requires a multidisciplinary approach. Considerations for total vertebrectomy should be discussed when direct invasion involves 30% or less of the vertebral cortical bone, with preoperative and postoperative chemoradiotherapy deemed sufficient for disease recurrence prevention [28].

In conclusion, the surgical management of lung cancer with spinal invasion is complex and controversial, potentially beneficial for severe pain management and tumour recurrence control [29,30]. Complete resection and multilevel laminectomy may be proposed for extensive tumour invasion, while partial vertebrectomy is suggested for less extensive tumour involvement. This underscores the need for aggressive, multidisciplinary surgical strategies, particularly for superior sulcus tumours with vertebral invasion, to improve prognosis and survival rates [31-33].

DISCUSSION

Presently, lung cancer is acknowledged as one of the deadliest cancers, with spinal metastases deemed generally incurable. Metastatic spread to the thoracic spine from lung cancer, which can occur via lymphatic or hematogenous routes, is notably frequent [34]. The consideration of surgical intervention for metastatic lung cancer infiltrating the spine presents a formidable challenge, marked by debate. The characteristics of the metastasis, including the organs involved, extent of infiltration, number of bone metastases, severity of spinal cord impairment, and level of pain, are critical prognostic factors that influence both the surgical outcomes and the patient's survival prospects [34,35].

The prognosis plays a pivotal role in deciding the appropriateness of surgical intervention. Consequently, there's a notable hesitancy to opt for surgery in patients with a limited life expectancy, compounded by a scarcity of studies and data supporting surgical intervention in such patient demographics [35]. The prognostic scoring systems developed in the 1990s and early 2000s, such as the Tokuhashi score, are commonly utilised to assess patients with a grim prognosis. However, the reliability and predictive accuracy of these tools have been questioned, as they often fail to accurately forecast survival, leading to potential underutilization in surgical candidate selection [35,36]. Lee et al. highlighted that the actual survival of patients frequently surpassed the expectations set by the revised Tokuhashi score, suggesting an improvement in survival rates due to advancements in medical and surgical oncology, which complicates the prognosis prediction [37]. Therefore, it is crucial to reevaluate the exclusion criteria to ensure that patients who could benefit from surgery are not inadvertently overlooked.

In the surgical treatment planning process, spine surgeons should be mindful of the tendency to underestimate patient survival. Notably, patients who have not previously received systemic treatment might benefit more substantially from surgery. Factors such as low BMI, indicative of a cachectic state, may predict a worse prognosis and should be considered in the evaluation process. Ideal surgical candidates include those with adenocarcinoma amenable to targeted therapies, candidates for denosumab treatment, individuals in good general health, and those yet to undergo systemic treatments [23].

Historically, surgical treatment for lung cancer with spinal invasion has yielded disappointing long-term outcomes concerning both mortality and morbidity, particularly in advanced-stage patients. Such conditions have been characterised as incurable and unresectable, with a poor long-term prognosis, especially in cases of vertebral invasion by superior sulcus tumours [38]. However, Yokomise et al. reported that advancements in technology and the introduction of novel surgical techniques have

the potential to enhance surgical outcomes [32]. Recent studies have demonstrated the efficacy of multimodal treatment, including surgical resection for selected patients with superior sulcus tumours involving the spine, showcasing safe procedures with promising survival rates following concurrent chemoradiotherapy (CRT) and surgical resection, resulting in a 5-year overall survival (OS) and disease-free survival (DFS) rate of 55% and 40%, respectively [39].

Park et al. aimed to analyse survival and functional outcomes post-surgery in patients with spinal metastases and limited life expectancy, reviewing 492 surgical cases across different time frames. The study found a significant improvement in median survival, particularly in the latest period studied (2013–2020), with notable survival enhancements for lung and kidney cancer cases within this timeframe [40]. Moreover, hybrid therapy involving separation surgery followed by stereotactic body radiation therapy in NSCLC patients with metastatic epidural spinal cord compression has shown high local control rates and survival benefits when combined with Epidermal Growth Factor Receptor (EGFR) -targeted treatments initiated post-hybrid therapy [41].

A recent meta-analysis systematically reviewed prognostic factors and outcomes of surgical intervention for lung cancer patients with spinal metastases, covering 14 studies and 813 patients. The analysis identified preoperative ambulatory status and the number of involved vertebrae as significant prognostic factors influencing survival. The study suggests that patients with an adequate expected survival period could gain from surgical intervention, particularly when combined with adjuvant therapies [42].

Consequently, a deeper understanding of metastatic disease pathophysiology and technological advancements has the potential to refine surgical techniques, improving prognosis and extending survival for appropriately selected patient groups. Despite the constrained role of surgery in the overarching management of spinal metastatic disease from lung cancer, its potential benefits for specific patient cohorts should not be overlooked. Future perspectives should focus on refining patient selection criteria and enhancing surgical techniques through research and technological advancements. These efforts promise to better delineate the role of surgery within a multifaceted treatment approach, aiming for improved survival rates and quality of life for patients facing this challenging diagnosis.

CONCLUSION

The surgical approach, while not the universal standard, plays a pivotal role in the management of spinal metastatic disease from lung cancer for select patients. This necessitates precise diagnosis and tailored interventions, considering the disease's stage, patient's health, and symptom severity. Treatment strategies, often encompassing surgery, radiation, chemotherapy, and supportive care, aim to alleviate symptoms and enhance life quality. Identifying candidates for surgery requires a multidisciplinary approach, emphasizing the need for collaborative planning and evaluation by a team of specialists to ensure the most beneficial outcomes. Ongoing research is crucial to unravel the complexities of spinal metastasis and to innovate more effective treatments. Understanding the mechanisms of metastasis and improving therapeutic options will ultimately enhance patient management and prognosis. Thus, while surgery offers significant benefits for certain patients, its application should be carefully considered within a comprehensive, patient-focused, and multidisciplinary treatment framework.

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Conflict of interest: *There are no conflicts of interest to declare.*

REFERENCES

1. Papagelopoulos PJ, Savvidou OD, Galanis EC, Mavrogenis AF, Jacofsky DJ, Frassica FJ, et al. Advances and challenges in diagnosis and management of skeletal metastases. Orthopedics. 2006 Jul;29(7):609-20; Quiz 621-2.
2. Ratliff JK, Cooper PR. Metastatic spine tumors. South Med J. 2004 Mar;97(3):246-53.
3. Coleman RE. Metastatic bone disease: clinical features, pathophysiology and treatment strategies. Cancer Treat Rev. 2001 Jun;27(3):165-76.
4. Berenson JR, Rajdev L, Broder M. Managing bone complications of solid tumors. Cancer Biol Ther. 2006 Sep;5(9):1086-9.
5. Botteman M, Foley I, Marfatia A, Brandman J, Langer C. Economic value of Zoledronic acid versus placebo in the treatment of skeletal metastases in patients with lung cancer: The case of the United Kingdom (UK). J Clin Oncol. 2007 Jun;25(18_suppl):6617.
6. Sundaresan N, Digiacinto GV, Hughes JE, Cafferty M, Vallejo A. Treatment of neoplastic spinal cord compression: results of a prospective study. Neurosurgery. 1991 Nov;29(5):645-50.
7. Aydinli U, Ozturk C, Bayram S, Sarihan S, Evrensel T, Yilmaz HS. Evaluation of lung cancer metastases to the spine. Acta Orthop Belg. 2006 Oct;72(5):592-7.
8. Maisano R, Pergolizzi S, Cascinu S. Novel therapeutic approaches to cancer patients with bone metastasis. Crit Rev Oncol Hematol. 2001 Dec;40(3):239-50.

9. Peh WC, Muttarak M. Clinics in diagnostic imaging (82). Lesser trochanter metastasis. Singapore Med J. 2003 Feb;44(2):101-5.
10. Chen YJ, Chang GC, Chen HT, Yang TY, Kuo BI, Hsu HC, et al. Surgical results of metastatic spinal cord compression secondary to non-small cell lung cancer. Spine (Phila Pa 1976). 2007 Jul;32(15):E413-8.
11. Komagata M, Nishiyama M, Imakiire A, Kato H. Total spondylectomy for en bloc resection of lung cancer invading the chest wall and thoracic spine. Case report. J Neurosurg. 2004 Apr;100(4 Suppl Spine):353-7.
12. Patchell RA, Tibbs PA, Regine WF, Payne R, Saris S, Kryscio RJ, et al. Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: A randomised trial. Lancet. 2005 Aug;366(9486):643-8.
13. Jacobs WB, Perrin RG. Evaluation and treatment of spinal metastases: An overview. Neurosurg Focus. 2001 Dec;11(6):e10.
14. Zhang JX, Song ZR, Zou J, Ge J, Yang HL. Balloon kyphoplasty as palliative care for painful pathological spinal fracture followed by lung cancer metastasis: A cohort study. Front Surg [Internet]. 2023 Jan;9:1081823. Available from: https://pubmed.ncbi.nlm.nih.gov/36733676/
15. Wang Y, Liu H, Pi B, Yang H, Qian Z, Zhu X. Clinical evaluation of percutaneous kyphoplasty in the treatment of osteolytic and osteoblastic metastatic vertebral lesions. Int J Surg. 2016 Jun;30:161-5.
16. Bartels RH, van der Linden YM, van der Graaf WT. Spinal extradural metastasis: review of current treatment options. CA Cancer J Clin. 2008 Jul-Aug;58(4):245-59.
17. Weigel B, Maghsudi M, Neumann C, Kretschmer R, Müller FJ, Nerlich M. Surgical management of symptomatic spinal metastases. Postoperative outcome and quality of life. Spine (Phila Pa 1976). 1999 Nov;24(21):2240-6.
18. Tokuhashi Y, Matsuzaki H, Toriyama S, Kawano H, Ohsaka S. Scoring system for the preoperative evaluation of metastatic spine tumor prognosis. Spine (Phila Pa 1976). 1990 Nov;15(11):1110-3.
19. Tokuhashi Y, Matsuzaki H, Oda H, Oshima M, Ryu J. A revised scoring system for preoperative evaluation of metastatic spine tumor prognosis. Spine (Phila Pa 1976). 2005 Oct;30(19):2186-91.
20. Tomita K, Kawahara N, Kobayashi T, Yoshida A, Murakami H, Akamaru T. Surgical strategy for spinal metastases. Spine (Phila Pa 1976). 2001 Feb;26(3):298-306.
21. Leithner A, Radl R, Gruber G, Hochegger M, Leithner K, Welkerling H, et al. Predictive value of seven preoperative prognostic scoring systems for spinal metastases. Eur Spine J. 2008 Nov;17(11):1488-95.
22. Balain B, Jaiswal A, Trivedi JM, Eisenstein SM, Kuiper JH, Jaffray DC. The Oswestry Risk Index: an aid in the treatment of metastatic disease of the spine. Bone Joint J. 2013 Feb;95-B(2):210-6.
23. Huang AP, Yang CY, Xiao F, Yang SH, Chen CM, Lai DM, et al. Spinal metastases from non-small cell lung cancer - Is surgical extent enough by following suggestions of the Tomita and Tokuhashi scores? Asian J Surg. 2023 Sep:S1015-9584(23)01332-5.
24. Hansen BH, Keller J, Laitinen M, Berg P, Skjeldal S, Trovik C, et al. The scandinavian sarcoma group skeletal metastasis register. Survival after surgery for bone metastases in the pelvis and extremities. Acta Orthop Scand Suppl. 2004 Apr;75(311):11-5.
25. Katagiri H, Takahashi M, Wakai K, Sugiura H, Kataoka T, Nakanishi K. Prognostic factors and a scoring system for patients with skeletal metastasis. J Bone Joint Surg Br. 2005 May;87(5):698-703.
26. van der Linden YM, Dijkstra SP, Vonk EJ, Marijnen CA, Leer JW. Dutch Bone Metastasis Study Group. Prediction of survival in patients with metastases in the spinal column: results based on a randomized trial of radiotherapy. Cancer. 2005 Jan;103(2):320-8.
27. Sartori F, Rea F, Calabrò F, Mazzucco C, Bortolotti L, Tomio L. Carcinoma of the superior pulmonary sulcus. Results of irradiation and radical resection. J Thorac Cardiovasc Surg. 1992 Sep;104(3):679-83.
28. Rusch VW, Giroux DJ, Kraut MJ, Crowley J, Hazuka M, Johnson D, et al. Induction chemoradiation and surgical resection for non-small cell lung carcinomas of the superior sulcus: Initial results of Southwest Oncology Group Trial 9416 (Intergroup Trial 0160). J Thorac Cardiovasc Surg. 2001 Mar;121(3):472-83.
29. Ginsberg RJ, Martini N, Zaman M, Armstrong JG, Bains MS, Burt ME, et al. Influence of surgical resection and brachytherapy in the management of superior sulcus tumor. Ann Thorac Surg. 1994 Jun;57(6):1440-5.
30. Komaki R, Mountain CF, Holbert JM, Garden AS, Shallenberger R, Cox JD, et al. Superior sulcus tumors: Treatment selection and results for 85 patients without metastasis (Mo) at presentation. Int J Radiat Oncol Biol Phys. 1990 Jul;19(1):31-6.
31. Grunenwald DH, Mazel C, Girard P, Veronesi G, Spaggiari L, Gossot D, et al. Radical en bloc resection for lung cancer invading the spine. J Thorac Cardiovasc Surg. 2002 Feb;123(2):271-9.
32. Yokomise H, Gotoh M, Okamoto T, Yamamoto Y, Ishikawa S, Liu D, et al. En bloc partial vertebrectomy for lung cancer invading the spine after induction chemoradiotherapy. Eur J Cardiothorac Surg. 2007 May;31(5):788-90.
33. Spaggiari L, Rusca M, Carbognani P, Solli P. Hemivertebrectomy for apical chest tumors: is the risk justified by the outcome? Ann Thorac Surg. 1998 May;65(5):1515-7.
34. Kaloostian PE, Zadnik PL, Etame AB, Vrionis FD, Gokaslan ZL, Sciubba DM. Surgical management of primary and metastatic spinal tumors. Cancer Control. 2014 Apr;21(2):133-9.
35. Dea N, Versteeg AL, Sahgal A, Verlaan JJ, Charest-Morin R, Rhines LD, et al. Metastatic Spine Disease: Should Patients With Short Life Expectancy Be Denied Surgical Care? An International Retrospective Cohort Study. Neurosurgery. 2020 Aug;87(2):303-11.
36. Tabourel G, Terrier LM, Dubory A, Cristini J, Nail LL, Cook AR, et al. Are spine metastasis survival scoring systems outdated and do they underestimate life expectancy? Caution in surgical recommendation guidance. J Neurosurg Spine. 2021 Jul;35(4):527-34.
37. Lee BH, Kim TH, Chong HS, Moon ES, Park JO, Kim HS, et al. Prognostic factor analysis in patients with metastatic spine disease depending on surgery and conservative

treatment: review of 577 cases. Ann Surg Oncol. 2013 Jan;20(1):40-6.
38. Oka S, Matsumiya H, Shinohara S, Kuwata T, Takenaka M, Chikaishi Y, et al. Total or partial vertebrectomy for lung cancer invading the spine. Ann Med Surg (Lond). 2016 Oct;12:1-4.
39. Unal S, Feller R, Stadhouder A, Heineman DJ, Jiya TU, van Dorp M, et al. Superior sulcus tumors invading the spine: multimodal treatment outcomes from the pre-immunotherapy era. JTO Clin Res Rep [Internet]. 2023 Oct;4(12):100582. Available from: https://pubmed.ncbi.nlm.nih.gov/38046379/
40. Park SJ, Ma CH, Lee CS, Jeon CY, Shin TS, Park JS. Survival and functional outcomes after surgical treatment for spinal metastasis in patients with a short life expectancy. J Clin Med. 2022 Dec;12(1):46.
41. Chakravarthy VB, Schachner B, Amin AG, Reiner AS, Yamada Y, Schmitt A, et al. The impact of targetable mutations on clinical outcomes of metastatic epidural spinal cord compression in patients with non-small-cell lung cancer treated with hybrid therapy (Surgery Followed by Stereotactic Body Radiation Therapy). Neurosurgery. 2023 Mar;92(3):557-64.
42. Zheng J, Ding X, Wu J, Li L, Gao X, Huang Q, et al. Prognostic factors and outcomes of surgical intervention for patients with spinal metastases secondary to lung cancer: An update systematic review and meta analysis. Eur Spine J. 2023 Jan;32(1):228-43.

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Introducing a robotic surgery program in the Greek National Healthcare System: Obstacles we need to overcome

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ABSTRACT

A National Healthcare Systems' primary objective is to ensure equal access to its members. Every advancement in medicine, which has proven to be safe and efficient, must be provided to every patient regardless of their socioeconomic background or financial status. However, the systems' nonprofit guiding principle results in inadequate financial support, which generates a vicious cycle of disproportionate access to its resources. A recent technological breakthrough in surgery, with several bestowed advantages, is the robotic surgical platform. However, its implementation in the Greek National Healthcare System, for the common good, is associated with several obstacles. The purpose of this article is to outline these obstacles and to suggest potential solutions, in order to eliminate any disparities between patients operated in public or private sector hospitals.

Key Words: *Greek national healthcare system, robotic surgery, financial obstacles*

The principal factor for the development of a robotic surgical platform has been the constant need to undertake surgical tasks requiring tremendous manual dexterity and technical skills, whilst minimising human error and improving patient outcomes [1]. The adoption of a robotic assisted surgery (RAS) program, within a wide spectrum of surgical specialties including gynaecology, urology and general surgery, has several bestowed advantages. These include the minimisation of surgical trauma, earlier mobilisation, decreased postoperative morbidity rates and a shorter length of hospital stay (LOS) [2,3,4,5,6]. Multiple national and international reports have shown a notable increase in the use of RAS across multiple surgical specialties and subspecialties over the past decade. In a previous report, we had highlighted a similar increase in the number of robotic surgical procedures performed in Greece between 2007 and 2017. Currently, there are seventeen robotic surgical systems in operation in Greece. Out of them 13 are located in Athens and four in Thessaloniki. Nonetheless, only two are purchased by the Greek National Healthcare System and operate in public hospitals, while the rest operate in private hospitals. This highlights the major issues associated with the funding of a robotic surgical program, on the one hand, and on the other hand the disparities in the quality of healthcare services between the public and private sector. Hence, it is important to understand that setting up a cutting-edge robotic surgery platform for general surgery procedures in a public hospital poses numerous obstacles that must be overcome [7]. The overall success of such a program lies within the implementation of a long-term business plan and setting a strict timeline which aim to overcome all the associated obstacles [8].

To date, the greatest disadvantage of robotic surgery remains its significant per capita cost [7]. A national network of patient referrals to expert centers, which is of

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cardinal importance in the field of surgical oncology for example, could act as a springboard for the establishment of a robotic surgery program. Greece is one of the four countries in Europe where a policy in the centralisation of surgery is absent. However, it is indicated from the literature, that referral for complex conditions in expert centers improves the quality and lowers the cost of the treatment provided [9]. Furthermore, the utilisation of the same robotic surgical platform by several surgical specialties and the ability to reuse the equipment, are the key elements of its sustainability. These strategic approaches might facilitate tackling the considerable per capita cost of obtaining and operating such a system [10].

Before starting a RAS program, it is crucial to establish a long term business development plan, of at least three years, with projected cost balances. This should include the direct (related to the robotic platform) and indirect (associated material, staff training) costs. The starting point of an efficient business plan, would be the foundation of a dedicated robotics committee within a hospital. Ideally, the committee should be composed of several individuals originating from the hospital staff, who can contribute to different lines of work: a hospital administrator, an anaesthesiologist, a surgeon, and a trained nurse. The composition of the robotics team, by various staff members with distinct roles, will eventually lead to an increased probability of success and provide a sounder transition once the program starts. Furthermore, establishing a national registry or even an institutional database is essential for the quality assessment of the program. Data analysts along with administrative staff could become valuable assets, guaranteeing the independent collection of data and its evaluation.

Initially, in order to have a robotic system operating at its full potential, it is necessary to construct a dedicated operating room (OR) with adequate space, equipped with specialised infrastructure including robotic consoles, instruments, and a three-dimensional imaging system. On the contrary, an existing OR has to be modified accordingly, in order to accommodate the surgeons' console, the robotic arms, anaesthesia equipment, operating table, instruments and auxiliary equipment while maintaining safe spaces for the circulating staff. However, modifying an existing operating room accordingly or even constructing a new one, poses a substantial logistical and financial challenge for a public hospital, adding to the cost of purchasing a robot [11].

Acquisition and maintenance of robotic surgical systems entail considerable expenses for a public hospital in Greece. Meticulous evaluation of the cost prior to the initial purchase, installation, maintenance, and ongoing instrument expenditures is of cardinal importance to ensure the preservation of a robotic surgery program. Public hospitals rely solely on funds derived from the national budget to operate. Given the fact that Greece's health expenditure per capita is less than half the average in the European Union (EU) [12], the task to secure funding for such a capital-intensive project is challenging.

Operating a robotic surgical system necessitates specialised training for the involved personnel. In the early years, surgeon training relied upon the companies manufacturing the robots. However, surgical organisations like the European Hernia Society and the European Society of Coloproctology for example, have realised the deficit in a structured training program for robotic surgery, and have established collaborative robotic training courses. This resulted in a formulated and scientifically validated training program, addressing the significant cost of training as well. In Greece there is absence of an established fellowship program in robotic surgery that could lead to a relevant certification. A handful of non-profit training centers provide young surgeons with simulation training. However, this is not established as part of a structured national training program. On the contrary, surgeons, surgical and nursing teams, as well as supporting staff, need to obtain continuous formal training, to ensure adequate operation and longevity of a robotic system. Ensuring a sufficient number of surgeons are trained in robotic colorectal, hepatobiliary, upper gastrointestinal and general surgery, as well as gynaecology and urology, is challenging. It requires additional funding from the hospitals' tight budget, and many man-hours subtracting from the hospitals' schedule. Furthermore, since there is a uniform pay scale among every physician of the same level working in Greece's National Health System, attracting skilled surgeons to work in a public hospital, by providing competitive financial income and career opportunities, may also prove daunting, if not absurd [13].

Avoidance of interruption of surgical waiting lists, resulting in delays in delivering safe and efficient surgery to patients, remains of cardinal importance. Thus, incorporating robotic surgery into the existing surgical workflow of a public hospital may be a multifaceted endeavour, which may require adjustments to scheduling, patient selection criteria, pre-operative preparation, post-operative care protocols and seamless coordination among different departments. Patient selection is one of the most crucial considerations in starting a successful robotics program. The properly selected patient should be someone who (a) can withstand a prolonged operative time, (b) presents with benign pathology and/or absence of significant inflammation (e.g., a large polyp of the rectosigmoid or

rectal prolapse), (c) has favourable anatomy (e.g. female pelvic anatomy provides a broad and wide pelvis versus the deep, narrow pelvis of a male), and (d) has no previous surgery (abdominal compartment free of adhesions). On the other hand, setting a predefined number of robotic operations on a weekly basis is also mandatory; hence a continuous flow of cases results in the improvement of the teams' experience.

Eliminating potential disparities and ensuring equal access to robotic surgery for all patients, regardless of their socioeconomic background, is another fundamental consideration associated with the moral structure of the national healthcare system. Providing equivalent distribution of resources and mitigating potential disparities in access, remains challenging, associated with the non-profit character of public hospitals. The necessity for regular maintenance, calibration, and software updates, as well as adequate technical support are indispensable to minimise downtime and ensure the longevity of the robotic platform. Thus, emanant resource limitations leading to inadequate maintenance and poor technical support, may undermine the longevity of the program.

Thoroughly evaluating the cost-effectiveness and clinical outcomes of establishing a robotic surgical program for colon and rectal procedures, initially, is imperative. Public hospitals must carefully assess whether the benefits offered by robotic surgery truly justify the initial investment. A potential solution would be to divide the significant per capita cost among different surgical specialties. Tertiary hospitals with multiple surgical specialties (e.g. urology, gynaecology, transplantation), where a wide variety of robotic procedures could be undertaken, would benefit the most. That distribution would eventually minimise the cost per procedure, and lead to a higher number of patients benefiting from the robotic approach. Moreover, there are several robotic platforms currently available on the market, developed by competitive firms. This, along with a careful evaluation of their distinct characteristics, is a key aspect in decreasing the cost of the initial purchase.

Addressing the aforementioned challenges effectively, necessitates a comprehensive approach involving collaboration among hospital administrators, surgeons, engineers and financial departments. A robotic surgery program is highly unlikely to be cost effective within the first year of operation and most probably will generate high costs within that period. Seeking external funding sources and forging partnerships with industry, academic institutions, or other healthcare organisations may contribute to overcoming the obstacles associated with establishing a robotic surgery platform in a public hospital. Perseverance, close collaboration between surgical teams and hospital management and a continuous

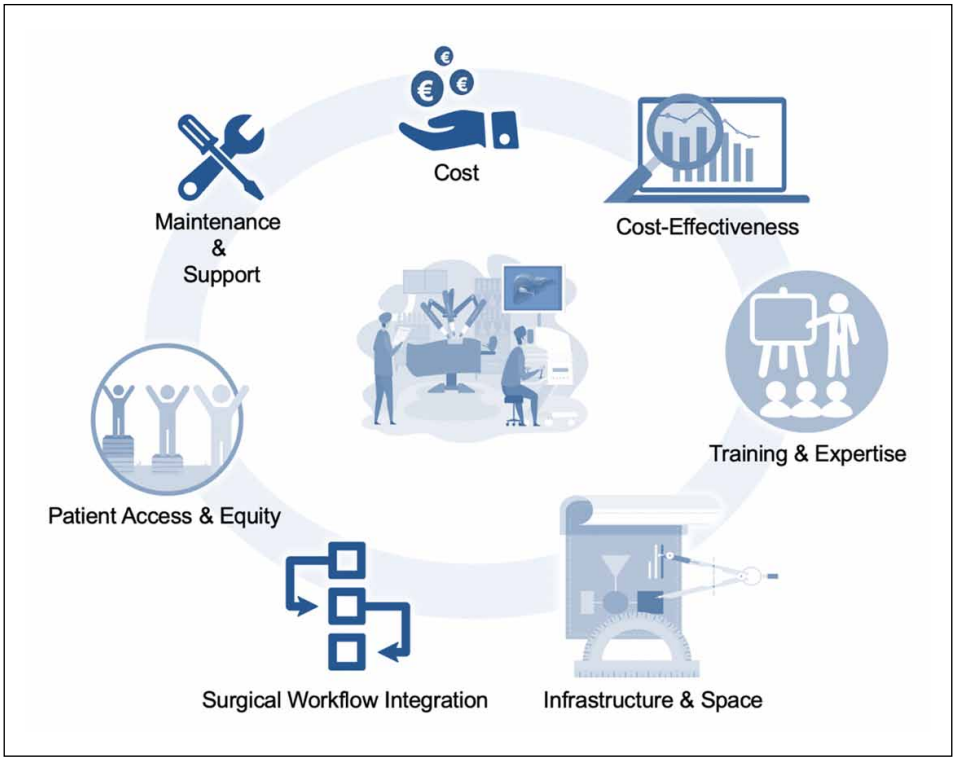

FIGURE 1. Schematic representation of the major contributing factors to a successful robotic surgical program.

strive to overcome all the aforementioned challenges, is the blueprint to the next success story in Greece's national healthcare system (Figure 1).

Ethical standards declaration: *Nothing to declare.*

Conflict of interest: *The authors declare no conflict of interest.*

REFERENCES

1. Kwoh YS, Hou J, Jonckheere EA, Hayati S. A robot with improved absolute positioning accuracy for CT guided stereotactic brain surgery. IEEE Trans Biomed Eng. 1988 Feb;35(2):153-60.
2. Machairas N, Dorovinis P, Kykalos S, Stamopoulos P, Schizas D, Zoe G, et al. Simultaneous robotic-assisted resection of colorectal cancer and synchronous liver metastases: A systematic review. J Robot Surg. 2021 Dec;15(6):841-8.
3. Machairas N, Papaconstantinou D, Tsilimigras DI, Moris D, Prodromidou A, Paspala A, et al. Comparison between robotic and open liver resection: a systematic review and meta-analysis of short-term outcomes. Updates Surg. 2019 Mar;71(1):39-48.
4. Doulamis IP, Spartalis E, Machairas N, Schizas D, Patsouras D, Spartalis M, et al. The role of robotics in cardiac surgery: a systematic review. J Robot Surg. 2019 Feb;13(1):41-52.
5. Ioannidis A, Kontzoglou K, Kouraklis G, Machairas N, Chrysoheris P, Antonakopoulos F, et al. Short-term outcomes in patients with colon cancer treated with robotic right colectomy. J BUON. 2018 Mar-Apr;23(2):317-21.
6. Doula C, Kostakis ID, Damaskos C, Machairas N, Vardakostas DV, Feretis T, et al. Comparison Between Minimally Invasive and Open Pancreaticoduodenectomy: A Systematic Review. Surg Laparosc Endosc Percutan Tech. 2016 Feb;26(1):6-16.
7. Steffens D, McBride KE, Hirst N, Solomon MJ, Anderson T, Thanigasalam R, et al. Surgical outcomes and cost analysis of a multi-specialty robotic-assisted surgery caseload in the Australian public health system. J Robot Surg. 2023 Oct;17(5):2237-45.
8. Ragupathi M, Haas EM. Designing a robotic colorectal program. J Robot Surg. 2011 Mar;5(1):51-6.
9. Vonlanthen R, Lodge P, Barkun JS, Farges O, Rogiers X, Soreide K, et al. Toward a consensus on centralization in surgery. Ann Surg. 2018 Nov;268(5):712-24.
10. Barry TM, Janjua H, DuCoin C, Eguia E, Kuo PC. Does adoption of new technology increase surgical volume? The robotic inguinal hernia repair model. J Robot Surg. 2022 Aug;16(4):833-9.
11. Giedelman C, Covas Moschovas M, Bhat S, Brunelle L, Ogaya-Pinies G, et al. Establishing a successful robotic surgery program and improving operating room efficiency: Literature review and our experience report. J Robot Surg. 2021 Jun;15(1):435-42.
12. OECD, Systems EOoH, Policies. Greece: Country Health Profile 20232023 [Internet]. Available from: https://www.oecd.org/greece/greece-country-health-profile-2023-dd530c3e-en.htm
13. Fieber JH, Kuo LE, Wirtalla C, Kelz RR. Variation in the utilization of robotic surgical operations. J Robot Surg. 2020 Aug;14(4):593-9.

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Repeated tracheal resection for endotracheal metastasis after sleeve pneumonectomy for squamous cell lung cancer

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ABSTRACT

The incidence of endotracheal and endobronchial metastases of both pulmonary and non-pulmonary primary malignancies is very rare. However, endotracheal metastasis may occur either as a result of recurrent lung cancer or of non-pulmonary originated neoplasia. Furthermore, reoperation on the trachea is a rare and challenging procedure. We here report a case of endotracheal metastasis from a squamous cell lung carcinoma, after previous tracheal sleeve pneumonectomy, which was resected via a "T" neck incision. The thorough observation of the trachea and bronchial tree over a long follow-up period is crucial for the early detection of endobronchial or endotracheal metastatic disease. Also, reoperation on the trachea can be carried out successfully by experienced surgeons.

Key Words: *Lung cancer; sleeve pneumonectomy; tracheal surgery; endotracheal metastasis*

INTRODUCTION

Endotracheal or endobronchial metastasis is a rare and potentially life-threatening entity and only few cases have been reported in the existing literature [1-3]. It may occur as a result of recurrent lung cancer or as distant metastasis of non-pulmonary neoplasia. Even up to 26% of endotracheal or endobronchial metastases may be due to colorectal cancer [4,5]. In contrast to the non-pulmonary endobronchial metastases, whose frequency has been clearly stated, lung originated tracheal metastasis has not been adequately studied due to its rarity. We report a case of endotracheal metastasis from a T4 No Mo squamous cell lung carcinoma, which had been treated by right sleeve pneumonectomy.

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CASE REPORT

A 53-year-old male patient was admitted to our hospital after a two weeks' history of persistent cough and mild

haemoptysis, and a history of previous thoracotomy for lung carcinoma. He had been diagnosed with squamous cell lung carcinoma and had undergone surgical treatment with right tracheal sleeve pneumonectomy, without post-operative chemotherapy. The initial tumour was located in the right upper lobe and extended to the right main bronchus omitted in less than 1,5 cm from the carina. Typical carinal resection along with right pneumonectomy was performed, with proper mediastinal lymphadenectomy of all paratracheal and subcarinal nodes, was accomplished. The size of the tumour was 3 x 2,7 x 1,7 cm, and no lymph nodes or remote metastases were detected. Resection was R0 and according to the final histology report, the stage of the disease was, despite the relatively small tumour size, T4N0M0. Following a straight forward postoperative recovery, he remained asymptomatic until he developed persistent cough, haemoptysis and respiratory distress nine months after surgery. Computed tomography (CT) scanning and rigid bronchoscopy were performed (Figures 1, 2). A nodule of maximum diameter of 0,8 cm was found in the middle-lower part of the trachea. Biopsies of the lesion were obtained through bronchoscopy. The histopathological results were compatible with squamous cell carcinoma and the nodule was therefore related to the primary squamous lung cancer and considered as a tracheal metastasis. The patient underwent additional tracheal resection, via a neck "T" incision with an upper sternotomy until the manubrium, and two cricoid cartilages of the middle-distal trachea were removed, followed by an end-to-end anastomosis, using single 4-0 vicryl stitches (Figure 3, 4). Frozen section showed free resection margins and histopathology revealed a region of 5 mm maximal diameter with high-grade dysplasia of squamous cell epithelium and disruption of the respiratory epithelial lining. The patient had an uneventful recovery and remained free of disease for the subsequent nine months. Routine postoperative evaluation revealed contralateral lung recurrence and supraclavicular and cervical lymph node dissemination. He was subsequently treated as a N3 stage patient with external radiation and chemotherapy (12 cycles of paclitaxel/carboplatin and 12 cycles of gemcitabine/vinorelbine). The patient had a moderate response to the treatment and died three years later.

FIGURE 1. Sagittal plane of the computed tomography showing the endotracheal metastasis (arrow).

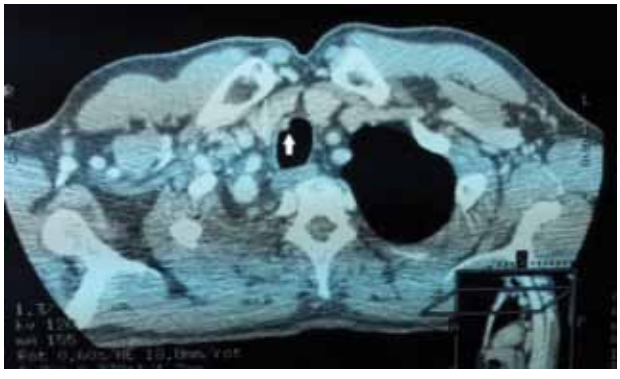

FIGURE 2. Transversal plane of the computed tomography showing the endotracheal metastasis (arrow).

DISCUSSION

Endotracheal or endobronchial metastatic disease can be a result of pulmonary or non-pulmonary neoplasias. The first report of endobronchial/endotracheal metastasis was published in 1971 by Schonbaum et al [6]. The incidence of metastases of non-pulmonary primary malignancies is 2-50% [4-8]. Carcinomas of the breast, kidneys, colon, uterus, the skin and sarcomas are the main primary tumours causing tracheobronchial metastases [8-11]. Trachea is involved in 0.5% of all the tumours of the tracheobronchial tree. There are only few cases of primary lung cancer endotracheal metastases reported in the current literature [1-3, 11-14], and only six reports as case series [2]. The majority of those cases were due to squamous cell carcinoma and nine cases of central type. Most of them have been traditionally treated with radiation therapy, chemotherapy, cryotherapy, brachytherapy and simple endoscopic resection, due to the coexistence of multiple synchronous metastases (lung parenchyma or

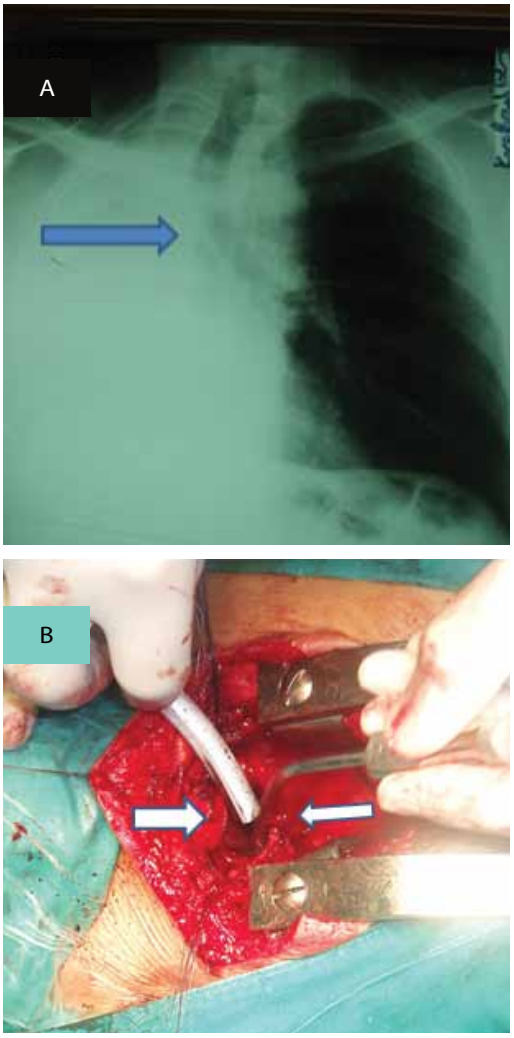

FIGURE 3. (A) Preoperative Chest X-ray after right sleeve pneumonectomy. Note the shift of mediastinum and the tracheal to left main bronchus anastomosis (arrow) made with 4-0 single vicryl stitches. (B) Operative illustration showing the tracheal edges after removal of the tumour (arrows). The two stumps were approximated with 4-0 vicryl stitches.

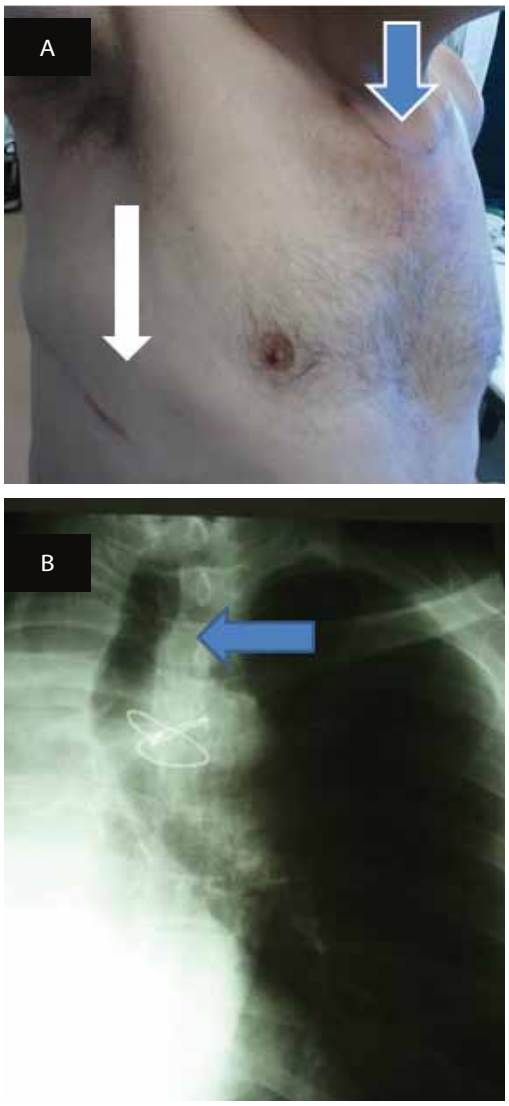

FIGURE 4. (A) Photo of the patient 3 weeks after second surgery, illustrating the two different incisions, thoracotomy for sleeve pneumonectomy (weight arrow) and "T" neck incision with partial upper minor sternotomy for resection of the endotracheal tumour (Blue arrow). (B) Chest radiography showing the tracheal anastomosis after tumour resection (arrow). Note the sternal figure of "8" wire for the approximation of the upper part of the sternum.

lymph node dissemination). Three of them were treated with tracheal resection and reconstruction with a recurrence interval of 8-52 months (mean 24,5 months). All cases were histopathologically identified as recurrences of known primary lung disease, except for 2 cases, where the tracheal metastasis revealed the disease [2]. A case of case of repeated endobronchial metastases of primary lung adenocarcinoma occurring 20 years after radical resection has also been reported [7]. The importance of the presence of lymphatic invasion in the primary tumour is also worth mentioning. In cases with negative lymph node metastasis, the time to recurrence is considered to be significantly longer compared to the positive cases [15]. Such patients with a history of lymphatic invasion present significantly higher recurrence rates than those without [1]. The prognosis of patients with endobronchial/endotracheal metastasis is generally considered poor [16]. Our case is to our knowledge the first documented case of tracheal sleeve pneumonectomy with tracheal recurrence, treated with additional tracheal resection and reconstruction, with the history of primary squamous lung cancer.

Cough, respiratory distress and haemoptysis are the most common symptoms of endotracheal metastases regardless of their primary origin [11]. CT scanning often reveals the presence of an endotracheal nodule or an

eccentric thickening of the tracheal wall. Additionally, virtual bronchoscopy with CT scanning of trachea can be a valuable diagnostic option for evaluation of tracheal tumours [17,18]. Fluorodeoxyglucose positron emission tomography (FDG-PET) has been suggested for the diagnosis of tracheal metastases and restaging of the disease [2,3]. Bronchoscopy performed by an experienced specialist could reveal the presence of small lesions. There are not any large series and long term results for none of the reported cases. Chong et al reported 6 cases of non-small cell lung cancer recurrence in the trachea. Five of those patients were treated with chemotherapy and radiation and only one with tracheal resection and end-to-end anastomosis [2]. All patients showed recurrence without exception. Radiation and chemotherapy resulted in a partial response slowing of the disease progression. There is no proven benefit of chemotherapy or radiation therapy over the surgical approach [2,16].

CONCLUSION

In conclusion, the incidence of endotracheal metastasis should always be considered in the differential diagnosis of respiratory symptoms in any patient with a positive history for malignancy, even after a long period after surgical treatment. Endoscopy and CT scanning can verify the diagnosis. Surgical approach is recommended and may improve survival for selected patients. Finally, as it was shown in our case, despite a previous carinal resection, reoperation on the trachea with additional cartilage removal can be safely performed by experienced surgeons. In all cases, a thorough and careful follow up is always recommended.

Ethical standards declaration: *Consent form: Was obtained from the patient for publication of this case report.*

Conflict of interest: *Authors report no conflict of interests.*

REFERENCES

1. Maki Y, Kimizuka Y, Sasaki H, Yamamoto T, Watanabe C, Sano T, et al. Lung adenocarcinoma with repetitive endotracheal/endobronchial metastasis 20 years after surgery: A case report. Thorac Cancer. 2021 Jan;12(1):133-6.
2. Chong S, Kim TS, Han J. Tracheal metastasis of lung cancer: CT findings in six patients. AJR Am J Roentgenol 2006 Jan;186(1):220-4.
3. Zhang Z, Mao Y, Chen H, Dong J, Yang L, Zhang L, et al. Endotracheal and endobronchial metastases in a patient with stage I lung adenocarcinoma. Ann Thorac Surg 2014 May; 97(5): e135-7.
4. Rosado Dawid NZ, Villegas Fernández FR, Rodríguez Cruz Mdel M, Ramos Meca A. Endobronchial metastases of colorectal cancer. Rev Esp Enferm Dig. 2016 Apr;108(4):232-3.
5. Serbanescu GL, Anghel RM. Can endobronchial or endotracheal metastases appear from rectal adenocarcinoma? J Med Life. 2017 Jan-Mar;10(1):66-9.
6. Schoenbaum S, Viamonte M. Subepithelial endobronchial metastases. Radiology 1971 Oct;101(1):63-9.
7. Rusca A, Carbognani P, Cattelani L, Spaggiari L, Solli P, Bobbio P. An uncommon indication for tracheal resection. J Cardiovasc Surg (Torino). 1996 Feb;37(1):89-91.
8. Marchioni A, Lasagni A, Busca A, Cavazza A, Agostini L, Migaldi M, et al. Endobronchial metastasis: An epidemiologic and clinicopathologic study of 174 consecutive cases. Lung Cancer 2014 Jun;84(3):222-8.
9. Kawahara K, Shiraishi T, Okabayashi K, Iwasaki A, Yoshinaga Y, Hayashi K, et al. Carinal resection and reconstruction for recurrent lung cancer. Surg Today 1997;27(2):163-5.
10. Oura S, Sakurai T, Yoshimura G, Tamaki T, Umemura T, Kokawa Y. Recurrent squamous-cell lung cancer treated with bronchial-arterial infusion of docetaxel-case report. Gan To Kagaku Ryoho. 1998 Nov;25(13):2109-13.
11. Kiryu T, Hoshi H, Matsui E, Iwata H, Kokubo M, Shimokawa K, et al. Endotracheal/endobronchial metastases: Clinicopathologic study with special reference to developmental modes. Chest. 2001 Mar; 119(3):768-75.
12. Ishiyama T, Aoyama T, Hirahara H, Iwashima A, Tsukada H, Souma T. Successful resection of endotracheal metastatic lung cancer using percutaneous cardiopulmonary support system: A case report. Kyobu Geka. 2001 Jan; 54(1):19-23.
13. De S. Tracheal metastasis of small cell lung cancer. Lung India 2009 Oct;26(4):162-4.
14. Tan CG, Shen L, Garske L, Tran K. Concurrent acute endobronchial and endotracheal tumor embolism. Thorax. 2010 Apr;65(5):464.
15. Mimae T, Tsutani Y, Miyata Y. Role of lymphatic invasion in the prognosis of patients with clinical node-negative and pathologic node-positive lung adenocarcinoma. J Thorac Cardiovasc Surg. 2014 Jun;147(6):1820-6.
16. Lu M, Zhu X, Cao B, Shen N. Investigation and Analysis of Primary Lung Cancer with Endotracheal and Endobronchial Metastases. Zhongguo Fei Ai Za Zhi. 2020 Mar;23(3):162-7.
17. Koletsis EN, Kalogeropoulou C, Prodromaki E, Kagadis GC, Katsanos K, Spiropoulos K, et al. Tumoral and non-tumoral trachea stenoses: evaluation with three-dimensional CT and virtual bronchoscopy. J Cardiothorac Surg. 2007 Apr;2:18.
18. Kagadis GC, Patrinou V, Kalogeropoulou CP, Karnabatidis D, Petsas T, Nikiforidis GC, et al. Virtual endoscopy in the diagnosis of an adult double tracheal bronchi case. Eur J Radiol. 2001 Oct;40(1):50-3.

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Goblet cell appendiceal adenocarcinoma. How to deal with this rare entity. Case report & review of literature

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ABSTRACT

Goblet Cell Adenocarcinoma (GCA) is considered a very rare entity with an incidence of 0.05 cases/100.000 per year. The aim of this report is the presentation of a case of 68-year old male who was diagnosed with GCA with a concomitant review of the recent literature. A 68 year old male presented in ED with a clinical and radiological appearance of acute appendicitis. The patient underwent a laparoscopic appendectomy. Biopsy of the specimen revealed GCA. A right hemicolectomy was performed one month later with an uneventful post-op course, followed by adjuvant chemotherapy due to one positive lymph node. A research on recent literature was performed focusing on clinical presentation, epidemiology, diagnosis, pathology, management and survival of patients with GCA. It revealed that GCA is usually first presented as acute appendicitis with the diagnosis being set only after histology report. It is not yet well established which grading system of colon cancer is more appropriate for this entity. Thus, although right hemicolectomy seems to be the treatment of choice, there are no clear guidelines about the surgical treatment of these patients. The 5 year old survival presents a great fluctuation according to tumor stage but in general it seems to be better than the one of adenocarcinoma of the colon.

Key Words: *Appendiceal tumours, appendicitis, goblet cell adenocarcinoma*

INTRODUCTION

Goblet cell adenocarcinoma of the appendix (GCA) is considered a very rare entity, according to literature, found in 0.05 cases/100,000 population per year. This tumour histopathologically resembles both adenocarcinomas and carcinoids, however showing a more aggressive attitude compared to them. Because of its unexpected course, which can vary from benign and slow-growing tumour to an aggressive malignant tumour, it needs careful assessment. There is still controversy whether radical surgery (Rt. Hemicolectomy) is needed, together with adjuvant chemotherapy. This mucus-secreting tumour is usually presented with abdominal pain mimicking clinical features of acute appendicitis [1]. In this abstract, we present a case report and we review the literature about this rare malignancy.

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CASE PRESENTATION

A 68-year-old male presented in ED, complaining of right lower quadrant abdominal pain. He also had a fever of 38.8 C, and his white blood cell count was abnormal (18.000). His clinical appearance imitated acute appendicitis. Abdominal CT scan was performed, which showed distended and inflamed appendix with possible rupture (Figure 1). During laparoscopy, the appendix was located retrocecal adherent to itself and the lateral abdominal

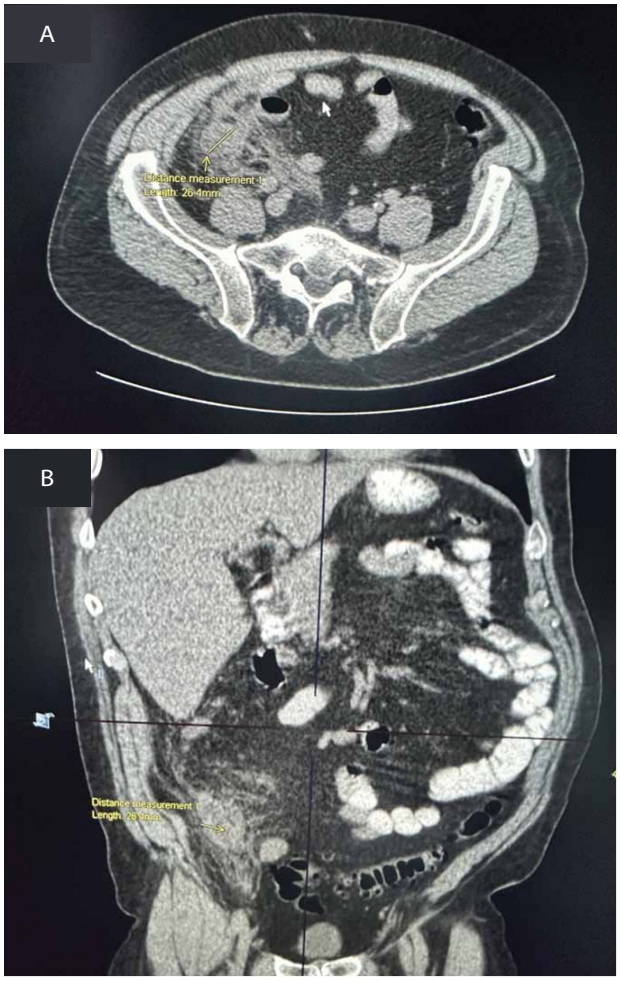

FIGURE 1. CT showing enlarged appendix and pericolic fat thickening.

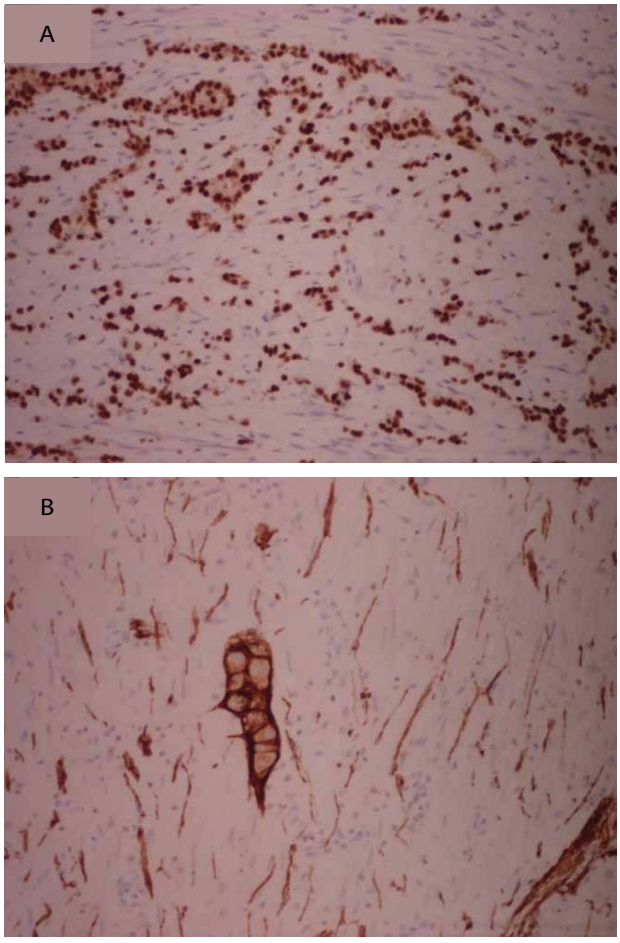

FIGURE 2. A: CDX-2 x 100 strain. B: CD56 X100 strain.

wall. Some purulent discharge was found around the area of inflammation. Meticulous dissection was performed and during mobilization, perforation of the apex of the appendix was found.

Laparoscopic appendectomy was performed using Harmonic endoshears (Ethicon) for the mesoappendix and 45mm GIA stapler with gold tape, stapling the base of appendix. Thorough lavage of the abdominal cavity was also performed. Patient's course following surgery was uneventful and he was discharged two days later. Biopsy of the specimen showed a 3 cm Goblet cell adenocarcinoma located mainly on the base of the appendix, extending to proximal margin of resection. Tumour was infiltrating mucosa, submucosa, muscularis propria but not the serosa. Additionally, findings of acute appendiceal inflammation with perforation at the apex were confirmed. Immunohistologic studies showed CDX2 (+), CK8-18 (+), CK7 (-), CD56 (+), Chromographin (+) and Synaptophysin (+) (Figures 2,3). Specimen was signed as GCA pT3NXR1.

A full colonoscopy was performed, in order to exclude other lesions in the rest of the bowel. After the MDT meeting, it was decided initially to proceed with right hemicolectomy. The operation was performed 30 days post appendectomy. An open limited right hemicolectomy was performed, with an uneventful post-op course. The patient was discharged seven days later. Biopsy of the specimen confirmed presence of GCA, on the appendiceal stump, extending 1.8cm in the cecum, infiltrating mucosa, submucosa, muscularis propria but not the serosa. Out of 28 lymph nodes removed, 1 was found positive (pT3N1). Patient started adjuvant chemotherapy 30 days post-op and 1 year follow-up since last operation, he is negative of tumour recurrence.

REVIEW OF THE LITERATURE

During review of the literature for GCA cases, we found interesting data regarding its clinical presentation, epidemiology, diagnosis, therapeutic management, histopathology & genetics, grading, prognosis and survival.

a. Clinical presentation: In most cases GCA presents as

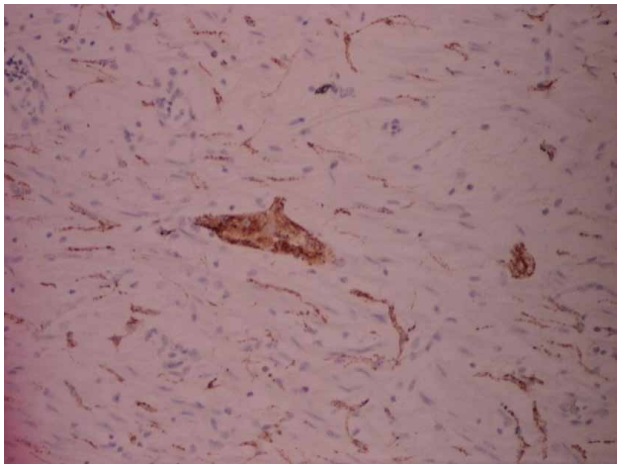

FIGURE 3. Synaptophysin X100 strain.

acute appendicitis. A high incidence of appendiceal perforation is reported, around 20-23% [2]. Appendicitis usually is related to low grade and localised disease. In the rest of the cases GCA could mimic non-specific abdominal pain or even abdominal mass, and in these cases most of the times we find high grade or metastatic disease. The most common sites of metastases are the liver, the small bowel and the ovaries. Regarding the location of the tumour within the appendix, no specific incidence in location (base, middle, apex) was documented in multiple studies [3-7].

b. **Epidemiology**: From literature, it is obvious that GCA is a quite uncommon entity, presenting with an incidence of 0.05-0.3 per year, per 100,000 cases. However some studies show an increased tendency of GCA recently [8]. GCA is more commonly found in Caucasian people (80-90%), with mean and median age at diagnosis reported between 50-60 years old [9].

c. **Diagnosis**: Unfortunately it is not easy to diagnose GCA, prior to histology report. CT scan is considered the main diagnostic modality, but GCA has no specific radiological features to differentiate from acute appendicitis. In some studies it is mentioned that PET (Positron Emission Tomography) scans may have better sensitivity, while in some other studies, serum carcinoembryonic antigen (CEA) [10-11] does.

d. **Pathology & Grading**: Goblet Cell Adenocarcinoma comes from pluripotent intestinal crypt base stem cells, which show combined mucinous and neuroendocrine differentiation. Focal presence of goblet shaped epithelial cells with intracytoplasmic mucin, remains the distinctive histopathologic feature of GCA. GCA stains positive on PAS (periodic acid-Schiff) staining of mucin. Grade of GCA is an independent prognostic factor, however at the moment there is a conflict between histopathologists, which grading system is more accurate regarding GCA, proposing different grading systems. There is a tendency from most studies to adopt for GCA to be classified as an adenocarcinoma, using a 4-stage grading system [12-15].

e. **Management**: There are no clear guidelines regarding appropriate management of GCA. There are some studies which imply that for a small (<1cm), low grade and apex or middle of appendix localised tumour, only appendectomy is sufficient. However, this situation is very rare, thus most of the times, if not all, additional post-appendectomy surgery is needed and more specifically right hemicolectomy [16-18]. Unfortunately, recurrence can occur, despite extensive surgery, which in some studies ranges between 16-20% and with higher possibility when positive lymph nodes are found. Use of adjuvant chemotherapy in patients undergoing right hemicolectomy, or having positive lymph nodes, or in cases of perforated appendix with appendicular abscess, seems to improve fve-year survival [19]. Metastatic disease shows an unfavorable prognosis, with five-year survival rate in Stage IV, less than 19%. In such cases palliative chemotherapy similar to colonic adenocarcinoma is used [20].

f. **Survival**: Five-year survival for GCA according to stages is estimated for ***Stage I*** 91.1%-100%, for ***Stage II*** 67%-90,5%, for ***Stage III*** 36%-57% and for **Stage IV** 4.2%-18.9%. It is evident from reviewing the literature, that GCA has worse survival than appendiceal MEN, but better than that in colonic adenocarcinoma, signet ring cell adenocarcinoma and mucinous adenocarcinoma [21-23]. Regarding independent prognostic factors, age, grade and stage, possibly have some importance, while male sex, lymph node metastases and positive surgical margins have been related to decreased survival in stage I-III [24].

DISCUSSION

GCA is a quite rare entity, which exclusively affects the appendix. It seems that it has a more aggressive attitude than carcinoid tumours, with a shift towards colonic adenocarcinoma. It is found in 0.3-0.9 appendectomy specimens and 14-19% in primary appendiceal cancer specimens. Mean age of diagnosis is between 50-60 years old, with no predominance between males and females. Usually, it presents with signs of acute appendicitis, and in some cases it may even cause small bowel obstruction, or in disseminated disease, it may be accompanied by vague abdominal pain, which usually it may be missed by physicians. Rarely only appendectomy is adequate, being

most of the times necessary a secondary surgical procedure, right hemicolectomy with adjuvant chemotherapy in presence of positive lymph nodes. The 5-year overall survival depends on the stage of the disease, which in case of positive lymph nodes or progressed disease, is quite poor [25].

Conflict of interest: *The authors declare that they have no conflict of interest.*

Consent: *Written informed consent was obtained from the patient for the publication of this case report and accompanying images.*

Ethical aproval: *Ethical Approval was provided by the authors' institution.*

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REFERENCES

1. Zhang K, Meyerson C, Kassardjian A, Westbrook IM, Zheng W, Wang HI. Goblet cell carcinoid/carcinoma: An update. Adv Anat Pathol. 2019 Mar;26(2):75-83.
2. Kiyosawa N, Koyama M, Miyagawa Y, Kitazawa M, Tokumaru S, Soejima Y. Goblet cell adenocarcinoma of the appendix: A case report of three cases. Int J Surg Case Rep. 2023 May;106:108229
3. Sigley K, Franklin M, Welch S. Appendiceal goblet cell adenocarcinoma case report and review of the literature. Cureus. 2021 Feb;13(2):E13511.
4. McGory ML, Maggard MA, Kang H, O'Connell JB, Ko CY. Malignancies of the appendix: Beyond case series reports. Dis Colon Rectum. 2005 Dec;48:2264-71.
5. Shaib W, Krishna K, Kim S, Goodman M, Rock J, Chen Z, et al. Appendiceal neuroendocrine, goblet and signet-ring cell tumors: A spectrum of diseases with different patterns of presentation and outcome. Cancer Res Treat. 2016 Apr;48(2):596–604.
6. Tang LH, Shia J, Soslow RA, Dhall D, Wong WD, O'Reilly E, et al. Pathologic classification and clinical behavior of the spectrum of goblet cell carcinoid tumors of the appendix. Am J Surg Pathol. 2008 Oct;32(10):1429-43.
7. Rajack F, Abdulbaki R, Chen W. Goblet cell adenocarcinoma of the appendix: An incidental finding a rare tumor which was recently renamed in 2019 World Health Organization classification update. Am Clin Pathol. 2021 Oct;156(Suppl 1):70-1.
8. Mo S, Zhou Z, Ying Z, Dai W, Xiang W, Han L, et al. Epidemiology of and prognostic factors for appendiceal carcinomas: A Retrospective, Population-Based Study. Int J Colorectal Dis. 2019 Nov;34(11):1915-24.
9. Kowalsky SJ, Nassour I, AlMasri S, Paniccia A, Zureikat AH, Choudry HA, et al. Omission of right hemicolectomy may be safe for some appendiceal goblet cell adenocarcinomas: A survival analysis of the national cancer database. Ann Surg Oncol. 2021 Dec;28(13):8916-25.
10. Lee KS, Tang LH, Shia J, Paty PB, Weiser MR, Guillem JG, et al. Goblet cell carcinoid neoplasm of the appendix: Clinical and CT features. Eur J Radiol. 2013 Jan;82(1):85-9.
11. Wang G, Li Q, Chen W. Chemotherapy in the treatment of different histological types of appendiceal cancers: A SEER Based Study. BMC Cancer. 2021 Jul;21(1):778.
12. Tsang ES, McConnell YJ, Schaeffer DF, Lee L, Yin Y, Zerhouni S, et al. Outcomes of surgical and chemotherapeutic treatments of goblet cell carcinoid tumors of the appendix. Ann Surg Oncol. 2018 Aug;25(8):2391-99.
13. Van Eeden S, Offerhaus GJA, Hart AAM, Boerrigter L, Nederlof PM, Porter E, et al. Goblet cell carcinoid of the appendix: A specific type of carcinoma. Histopathology. 2007 Dec;51(6):763-73.
14. Macak J, Nemejcova K, Dvorackova J. Are goblet cell carcinoids a group of heterogeneous tumors? Biomed Papers. 2017 Sep;161(3):281-85.
15. Jedrzkiewicz J, Tateishi Y, Kirsch R, Conner J, Bischof D, McCart A, et al. Impact of referral center pathology review on diagnosis and management of patients with appendiceal neoplasms. Arch Pathol Lab Med. 2020 Jun;144(6):764-68.
16. Palmer K, Weerasuriya S, Chandrakumaran K, Rous B, White B, Paisey S, et al. Goblet cell adenocarcinoma of the appendix: A systematic review and incidence and survival of 1,225 Cases From an English Cancer Registry. Front Oncol [Internet]. 2022 Jul;12:915028. Available from: https://pubmed.ncbi.nlm.nih.gov/35903705/
17. Turaga KK, Pappas SG, Gamblin TC. Importance of histologic subtype in the staging of appendiceal tumors. Ann Surg Oncol. 2012 May;19(5):1379-85.
18. Clift AK, Kornasiewicz O, Drymousis P, Faiz O, Wasan HS, Kinross JM, et al. Goblet cell carcinomas of the appendix: Rare but aggressive neoplasms with challenging management. Endocr Connect. 2018 Feb;7(2):268–77.
19. Olsen IH, Holt N, Langer SW, Hasselby JP, Grønbæk H, Hillingsø J, et al. Goblet cell carcinoids: Characteristics of a danish cohort of 83 patients. PloS One [Internet]. 2015 Feb;10(2):e0117627. Available from: https://pubmed.ncbi.nlm.nih.gov/25671432/
20. McConnell YJ, Mack LA, Gui X, Carr NJ, Sideris L, Temple WJ, et al. Cytoreductive surgery with hyperthermic intraperitoneal chemotherapy: An emerging treatment option for advanced goblet cell tumors of the appendix. Ann Surg Oncol. 2014 Jun;21(6):1975-82.
21. Pape U, Perren A, Niederle B, Gross D, Gress T, Costa F, et al. ENETS consensus guidelines for the management of patients with neuroendocrine neoplasms from the jejuno-ileum and the appendix including goblet cell carcinoid, Neuroendocrinology. 2012;95(2):135-56.
22. Boudreaux JP, Klimstra DS, Hassan MM, Woltering EA, Jensen RT, Goldsmith SJ, et al. The NANETS consensus guideline for the diagnosis and management of neuroendocrine tumors: Well-differentiated neuroendocrine tumors of the jejunum, ileum, appendix, and cecum. Pancreas. 2010 Aug;39:753-66.
23. Taggart MW, Abraham SC, Overman MJ, Mansfield PF, Rashid A. Goblet cell carcinoid tumor, mixed goblet cell carcinoid-adenocarcinoma, and adenocarcinoma of the appendix: Comparison of clinicopathologic features and prognosis. Arch Pathol Lab Med. 2015 Jun;139(6):782-90.
24. Zheng M, Li T, Li Y, Zhang T, Zhang L, Ma W, et al. Survival

profile and prognostic factors for appendiceal mixed neuroendocrine nonneuroendocrine neoplasms: A SEER population-based study. Front Oncol [Internet]. 2020 Aug;10. Available from: https://www.frontiersin.org/journals/oncology/articles/10.3389/fonc.2020.01660/full

25. Lamarca A, Nonaka D, Lopez Escola C, Hubner RA, O'Dwyer S, Chakrabarty B, et al. Appendiceal goblet cell carcinoids: Management considerations from a reference Peritoneal Tumour Service Centre and ENETS Centre of Excellence. Neuroendocrinology. 2016;103:500-17.

Case Report

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Management of a large Stage 4 sacrococcygeal pressure injury with surgical debridement and Negative Pressure Wound Therapy

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ABSTRACT

Background: Pressure injuries, affecting millions annually, pose substantial challenges globally.

Aim: Presentation of the management of a patient with a large sacrococcygeal pressure injury in our tertiary hospital.

Case presentation: Our (case) study highlights the case of a 67-year-old male with severe comorbidities and a significant sacrococcygeal pressure injury managed through surgical debridement and negative pressure wound therapy (NPWT). The patient's condition, complicated by infection, necessitated tailored treatment. NPWT, applied for 80 days and followed by absorbent dressings, facilitated granulation tissue formation and wound closure within 162 days post-NPWT cessation.

Conclusion: The case underscores the efficacy of NPWT in conjunction with infection control strategies, offering insights into managing complex pressure injuries, especially in settings with limited surgical resources.

Key Words: *Pressure injury; sacrococcygeal pressure ulcer; negative pressure wound therapy; surgical debridement*

INTRODUCTION

Pressure injuries, previously termed pressure ulcers, remain a significant burden on individuals and society, impacting approximately 3 million adults annually in the United States alone [1]. They present a considerable financial concern for various stakeholders including society, healthcare services, insurers, and patients [2]. The prevalence of pressure injuries has a median rate of 10.8%, with studies showing a range from 4.6% to 27.2% [3].

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Pressure injuries stem from various factors: prolonged pressure, friction, moisture, and internal issues like malnutrition and anaemia [4]. Risk factors include reduced mobility, skin moisture, poor nutrition, and diminished sensation [5]. Advanced age, cognitive impairment, and health conditions exacerbate tissue damage. Prolonged pressure diminishes oxygen supply, leading to tissue breakdown [4]. Even short periods of immobility can trigger ulceration. Dysfunction in nervous regulatory mechanisms worsens blood flow control, contributing to ulcer formation [6]. Treatment approaches vary based on factors such as nutritional status, pressure injury location and size, patient comorbidities, presence of infection, and healthcare system capabilities [7]. Treatment options for pressure ulcers encompass various approaches, including thorough cleaning and debridement to eliminate dead tissue [8]. Specialised wound dressings like hydrocolloid

or alginate dressings are employed to foster healing. In some cases, antibiotics may be prescribed to address infection [8]. Surgical interventions, such as sharp surgical debridement or other advanced techniques, may be considered for cases requiring extensive tissue removal or exposure of underlying structures [8]. Additionally, negative pressure wound therapy (NPWT) can be effective for deep or infected ulcers, particularly those with exposed bone [9]. Negative pressure wound therapy (NPWT) has been used either as a primary treatment or bridging in the management of large pressure injuries, especially with the presence of infection [9]. In our case study, we present a 67-year-old male patient with severe comorbidities and a significant sacrococcygeal pressure injury and the management with surgical debridement and use of negative pressure wound therapy (NPWT).

CASE PRESENTATION

A 67-year-old Caucasian male was referred from a secondary care hospital at the Department of Internal Medicine of our tertiary hospital due to a recently established ischaemic stroke of the right parietal lobe, as well as newly diagnosed heart failure and atrial fibrillation. Regarding his past medical history, he has been suffering from diabetes mellitus type 2, hypertension and dyslipidemia. The Braden Score on initial evaluation was 15, which considers the patient at risk of developing pressure injuries [10]. On physical examination, the patient was bedridden, had lower extremity oedema and pressure injuries on both his thighs. He also had a large sacrococcygeal pressure injury (Figure 1a). The patient was haemodynamic stable and non-febrile. C-reactive protein (CRP) levels were 195mg/l (0-5 mg/l) and due to purulent material from the pressure ulcers, a diagnosis of soft tissue infection was made and intravenous piperacillin-tazobactam and daptomycin were administered. During his hospital stay, a computed tomography (CT) scan of the abdomen was performed with the presence of ascites which was aspirated. The culture from the ascitic fluid revealed Enterococcus faecium which was sensitive to Daptomycin.

A surgical evaluation of the patient's pressure ulcer was performed under local anaesthesia. Regarding the sacrococcygeal pressure ulcer, it was initially categorised as unstageable full-thickness pressure injury, as the

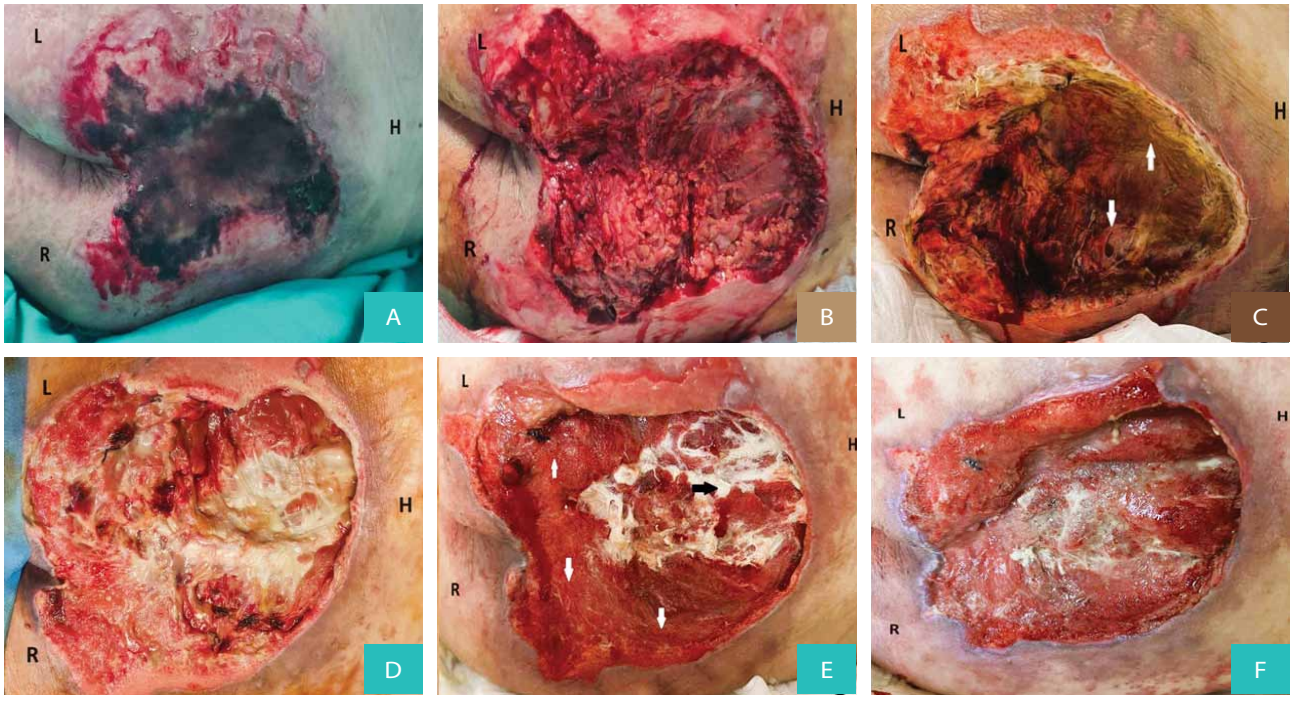

FIGURE 1. Patient's large sacrococcygeal pressure injury. A: On initial evaluation. Note the presence of eschar covering the wound. B: The wound after the 1st surgical debridement was categorised as stage 4. C: Two weeks after surgical debridement and initiation of negative pressure wound therapy, the pressure injury had new necrotic tissue formation (white arrows). A second surgical debridement was performed. D: On day 21 necrotic tissue was removed and wound cultures were sent. E: Pressure ulcer on patients discharge (Day 43). Note the granulation tissue (white arrows) and the presence of fibrous tissue over the sacrum (black arrow). F: The wound at the end of NPWT Day 80.
L: left lower limb, R: right lower limb, H: towards patient's head.

extent of the tissue damage within the ulcer could not be confirmed because it was obscured by slough and eschar. The ulcer seemed to extend into the muscles and other supporting structures including the fascia and the sacrum making osteomyelitis or osteitis likely to occur. The laboratory risk indicator for necrotising fasciitis (LRINEC) score was 3 [11]. Under local anaesthesia, surgical debridement was performed with removal of all necrotic tissues (Figure 1b). Tissue was also sent for culture which revealed a low bacterial load of Acinetobacter baumannii, Klebsiella pneumoniae (KPC), and Candida albigans. After surgical debridement, negative pressure wound therapy (NPWT) was applied on the wound surface using a pressure of 120mmHg (day 1). The sponge of the Vacuum Assisted Closure (VAC) system was replaced every two days and evaluation of the wound was performed. The patient's inflammation markers were improved. On day 14 due to the presence of necrotic tissue, a second surgical debridement took place and NPWT was used again (Figure 1c). On day 21, granulation tissue was present on nearly half of the surface area of the wound, except the areas where bony prominence was present (Figure 1d). A third surgical debridement of this area was performed and tissue was sent again for a culture that revealed a high bacterial load of Klebsiella pneumonia (KPC). For that reason, meropenem was administered for ten days. On day 23, the patient was febrile (39C) with elevation of the inflammation markers. Blood cultures revealed Clostiridium clostridiiforme bacteremia. Meropenem was replaced with metronidazole and the patient remained afebrile with normalisation of white blood cell counts and C-reactive protein (CRP) levels (Figure 2).

The patient was discharged on day 43 (Figure 1e) and he was referred to a rehabilitation center. NPWT was still used and the wound was evaluated every 3-4 days. No further surgical debridement was needed. NPWT was used until day 80 as it was replaced with highly absorbent alginate and foam dressings (Figure 1f). By day 103, the wound was covered with granulation tissue with newly formed skin tissue and the diameter of the deficit was gradually decreasing (Figure 3a). After 242 days, the wound was healed and the patient remains in excellent clinical condition (Figures 3b-d).

DISCUSSION

Pressure ulcers are a global issue, impacting approximately 1 to 3 million individuals in the United States each year. The incidence rates vary from 5% to 15% among hospitalised patients, with higher occurrences observed in intensive care units and specific long-term care settings [1]. A recent revision by the National Pressure Ulcer Advisory Panel (NPUAP) has brought changes to the definition and staging system of pressure ulcers [12]. The updated staging system replaces the term "ulcer" with "injury" and utilises Arabic numerals instead of Roman numerals to denote stages. The revised definition of a pressure injury now specifies that these injuries typically occur over bony prominences or beneath medical or other devices. Each definition outlines the extent of tissue loss and the anatomical characteristics that may or may not be present at

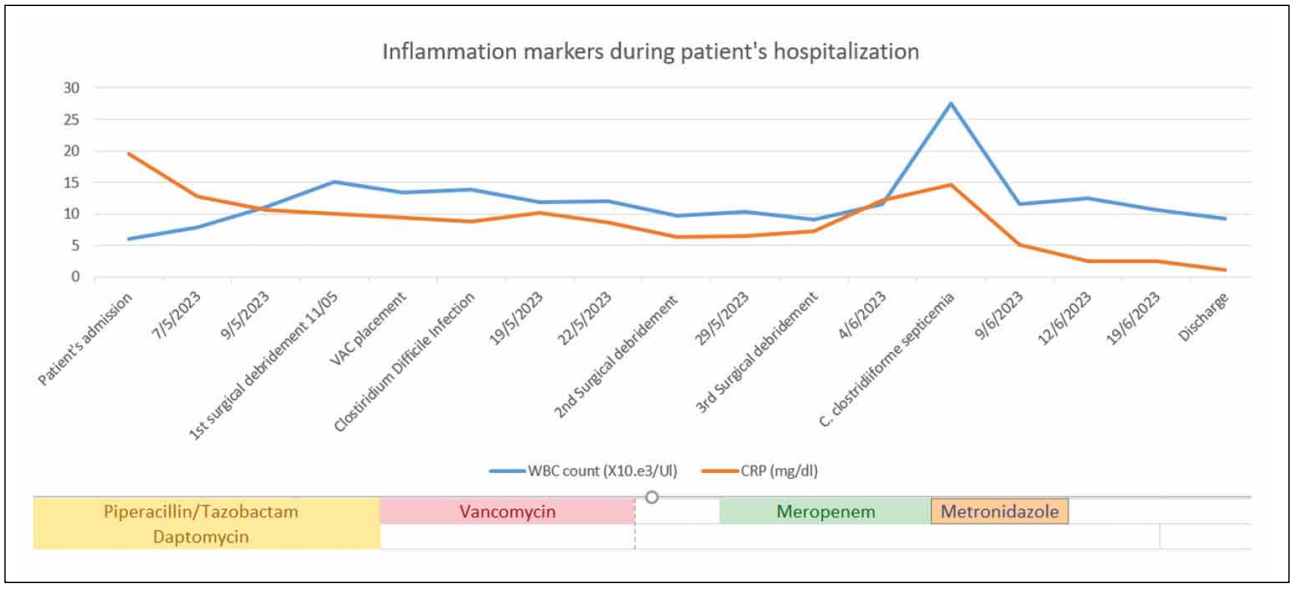

FIGURE 2. Inflammation markers (White Blood Cell-WBC count and C-reactive protein-CRP) during patient's hospitalization. The type and duration of antibiotics administered are also shown.

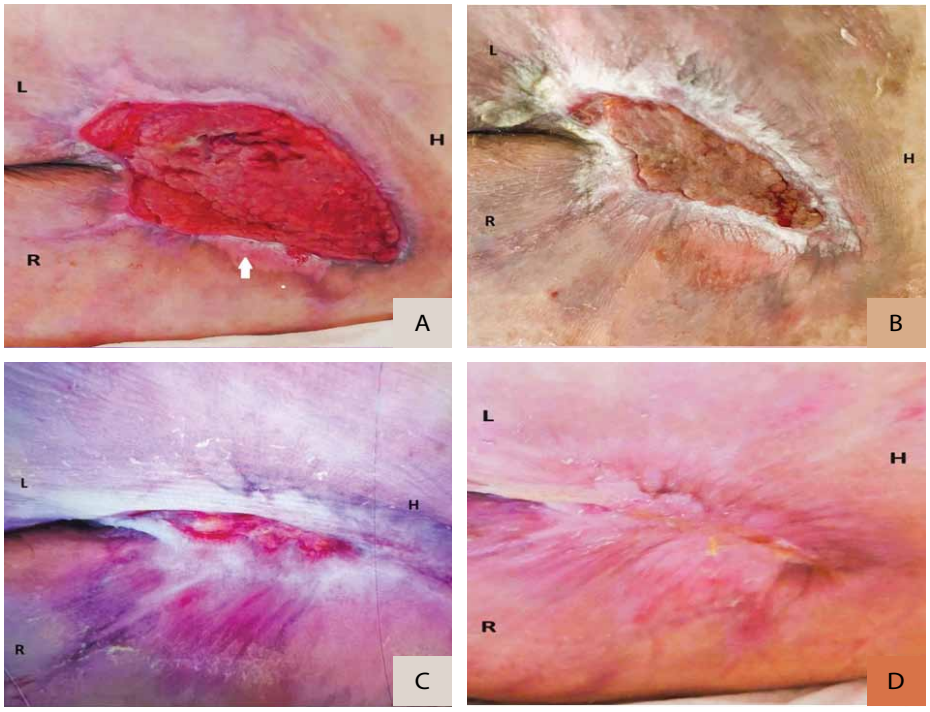

FIGURE 3. A: Day 103. Note the epithelization of the would ulcer (white arrow). B: Day 160. Highly absorbent alginate and foam dressings were used. C: Day 208 D: Day 242. The wound finally healed.
L: left lower limb, R: right lower limb, H: towards patient's head.

each stage of injury. Regarding the economical impact of pressure injuries, it is estimated that the cost of pressure ulcer prevention per patient at risk per day varied between 2.65 € and 87.57 € across all settings and the cost of pressure ulcer treatment per patient per day varied between 1.71 € to 470.49 € across all settings [2].

Treatment of Stage 1 and 2 pressure injuries includes the reduction of pressure and repositioning of the patient, utilisation of specialised support surfaces, decrease of friction, shear, and moisture, adequate nutrition, and dressing selection to promote moist wound healing [13]. Regarding stage 3 and 4 pressure injuries, treatment strategies are more complex. In addition to the aforementioned measures, negative pressure wound therapy may be utilised. Moreover, cell or tissue-based products and topical growth factors have been employed. Surgical techniques include primary closure if the injury is superficial and relatively small, debridement, and skin flap closure [13]. The appropriate method should be chosen based on various factors such as the patient's performance status, nutritional support, medical staff experience, and the availability of methods. In our case, the absence of a plastic surgery department precluded the ability to perform complex skin grafts. Conversely, negative pressure wound therapy was available as there was the capacity to replace the foam every 2-3 days and perform proper surgical debridement when necessary. All procedures were conducted bedside, thereby minimising the potential complications associated with receiving general anesthesia. The use of NPWT seems to be more effective in terms of granulation tissue formation and wound shrinkage compared to wet-to-dry dressing [14]. In our case, NPWT was applied for 80 days. After NPWT, highly absorbent alginate and foam dressings were used as there was no technical staff available to properly manage and evaluate vacuum-assisted closure (VAC) therapy. This management alteration may have changed the duration of the wound healing process, as the ulcer was finally healed 162 days after the discontinuance of VAC therapy.

Management of local infection is another important risk factor for delayed wound healing [9]. In our case, two wound cultures were taken. Antibiotics based on the antibiogram were administered only after the bacterial load increased, and the ulcer remained inflamed 20 days after the initial evaluation and surgical debridement. Inflammation markers were monitored, although they did not alter our therapeutic plan.

CONCLUSION

In this study, we present a case of a patient with medical comorbidities and a large stage 4 sacrococcygeal pressure injury. The combination of surgical debridement, use of negative pressure wound therapy and local infection control were used together and the wound despite the large size on initial evaluation was finally healed. Managing these patients involves a lengthy procedure that requires ongoing and meticulous clinical assessment, involving

diverse medical specialties like infectious diseases specialists within a multidisciplinary framework.

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Ethical Standards: *1) This case report has been approved by the hospital's ethics committee (Hippokrateion General Hospital) and has therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. 2) All persons gave their informed consent prior to their inclusion in the study.*

REFERENCES

1. Mervis JS, Phillips TJ. Pressure ulcers: Pathophysiology, epidemiology, risk factors, and presentation. J Am Acad Dermatol. 2019 Oct;81(4):881-90.
2. Demarre L, Van Lancker A, Van Hecke A, Verhaeghe S, Grypdonck M, Lemey J, et al. The cost of prevention and treatment of pressure ulcers: A systematic review. Int J Nurs Stud. 2015 Nov;52(11):1754-74.
3. Moore Z, Avsar P, Conaty L, Moore DH, Patton D, O'Connor T. The prevalence of pressure ulcers in Europe, what does the European data tell us: A systematic review. J Wound Care. 2019 Nov;28(11):710-19.
4. Zaidi SRH, Sharma S. Pressure Ulcer. StatPearls Treasure Island (FL): StatPearls Publishing [Internet]. 2024 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK553107/
5. Chou R, Dana T, Bougatsos C, Blazina I, Starmer AJ, Reitel K et al. Pressure ulcer risk assessment and prevention: A systematic comparative effectiveness review. Ann Intern Med. 2013 Jul;159(1):28-38.
6. van Marum RJ, Meijer JH, Ribbe MW. The relationship between pressure ulcers and skin blood flow response after a local cold provocation. Arch Phys Med Rehabil. 2002 Jan;83(1):40-3.
7. Gupta S, Ichioka S. Optimal use of negative pressure wound therapy in treating pressure ulcers. Int Wound J. 2012 Aug;9:(Suppl 1):8-16.
8. Bhattacharya S, Mishra RK. Pressure ulcers: Current understanding and newer modalities of treatment. Indian J Plast Surg. 2015 Jan-Apr;48(1):4-16.
9. Mouës CM, Vos MC, van den Bemd GJ, Stijnen T, Hovius SE. Bacterial load in relation to vacuum-assisted closure wound therapy: A prospective randomized trial. Wound Repair Regen. 2004 Jan-Feb;12(1):11-7.
10. Bergstrom N, Braden BJ, Laguzza A, Holman V. The Braden Scale for Predicting Pressure Sore Risk. Nurs Res. 1987 Jul-Aug;36(4):205-10.
11. Wong CH, Khin LW, Heng KS, Tan KC, Low CO. The LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis) score: a tool for distinguishing necrotizing fasciitis from other soft tissue infections. Crit Care Med. 2004 Jul;32(7):1535-41.
12. Edsberg LE, Black JM, Goldberg M, McNichol L, Moore L, Sieggreen M. Revised National Pressure Ulcer Advisory Panel Pressure Injury Staging System: Revised Pressure Injury Staging System. J Wound Ostomy Continence Nurs. 2016 Nov-Dec;43(6):585-97.
13. Mervis JS, Phillips TJ. Pressure ulcers: Prevention and management. J Am Acad Dermatol. 2019 Oct;81(4):893-902.
14. Şahin E, Rizalar S, Özker E. Effectiveness of negative-pressure wound therapy compared to wet-dry dressing in pressure injuries. J Tissue Viability. 2022 Feb;31(1):164-72.

Case Report

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Perineal hernia repair following tailgut cyst excision: A case report and literature review of optimal management strategies

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ABSTRACT

Perineal hernias, categorised as primary or secondary, pose a clinical challenge necessitating surgical intervention. Herein we present the surgical management of a postoperative perineal hernia of the retrorectal space. A 42-year-old female patient presented to the clinic with symptoms such as perineal discomfort, bulging, and constipation after previous surgical tailgut cyst excision. Diagnosis involved MRI, confirming rectal herniation into the retrorectal space. The surgical approach featured a perineal intervention using a unilateral inferior gluteal flap to reinforce the posterior rectal space, avoiding mesh complications. The patient experienced a successful recovery, highlighting the importance of tailored interventions based on symptoms and complications. Secondary perineal hernias, often postoperative, present diverse challenges influenced by multiple factors such as pelvic surgeries. Surgical repair options include perineal and abdominal approaches, mesh usage, and flap methods, each with variable outcomes. This case study contributes to the evolving understanding of perineal hernias, emphasising the need for multidisciplinary approaches and ongoing research to enhance management strategies in this complex clinical scenario.

Key Words: *Perineal; hernia; tailgut; cyst; repair*

INTRODUCTION

A perineal hernia (PH) refers to the protrusion of extraperitoneal or intraperitoneal contents into the perineum, resulting from a congenital or acquired defect of the pelvic floor muscles [1,2]. PHs can be classified into anterior and posterior according to their position in relation to the superficial transverse perineal muscle [3]. While PHs are generally infrequent, they can be categorised as primary or secondary. Primary PHs are linked to congenital and embryological deformities, whereas secondary hernias are acquired and usually arise postoperatively, particularly following major pelvic surgeries such as abdominoperineal resection (APR) [4]. The latter is the most prevalent and is characterised by symptoms such as presence of a palpable bulge, overlying skin erosions, abdominal pain, obstructive defecation symptoms and urinary disturbances [5].

Despite the rarity of PHs, a variety of surgical approaches have been employed for their treatment, triggering debates regarding the optimal choice that produces the most favourable outcomes with minimal complications [6]. Both abdominal and perineal approaches, along with the use of biological or synthetic mesh or flaps have been employed so far. These methods can be executed

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through open or endoscopic procedures, [7,8]. In this case study, we present the case of a posterior PH involving the herniation of the rectum into the retrorectal space after a tailgut cyst excision surgery. An informed consent was provided by the patient.

CASE PRESENTATION

A 42-year-old female patient presented in our clinic reporting three years of worsening perineal discomfort, posterior perineal bulging, lower back pain, chronic antalgic posture resulting in spondyloarthropathy and worsening constipation with the need of digital perineal support. The patient had never smoked and was slightly overweight (BMI 27 kg/m^2) with an unremarkable medical history, which included two physiologic labors and a surgical tailgut cyst excision, with partial coccyngectomy three years ago. Upon clinical examination, a soft mass was identified in the posterior perineal region, indicative of bowel herniation into the retrorectal space. Subsequent MRI of the lower abdomen revealed and confirmed the existence of a postoperative rectum herniation within the presacral space, specifically at the level of the S5 vertebra (Figure 1).

Surgical intervention was the treatment of choice for this perineal hernia, indicated by the aforementioned symptoms and the spondyloarthropathy resulting from the chronic antalgic posture. A bag enema was administered for bowel preparation the day before surgery. A longitudinal procedure was performed and a perineal sac with the underlying posterior rectal wall was detected (Figure 2). The gluteal fascia was detected and prepared bilaterally. Because of the very thin layer of the sac and to avoid possible mesh erosion any fistulization in the future, the use of perineal mesh was not preferred. The posterior rectal space was reinforced with a unilateral inferior gluteal flap. The flap was prepared from the right side, part of the skin was excised and got positioned deeply to get attached to the opposite gluteal muscle fascia (Figure 3). With this technique, there is a strong support against posterior herniation, with the advantages of avoiding mesh complications. Because of the extra traction forces at this part of the body, a double suture technique was chosen. A suction drain was placed and was removed on the third postoperative day. Patient had an uneventful recovery, well healing and on postoperative review demonstrated great improvement and comfortable seating, as well as no obstructing defacation symptoms (Figure 4).

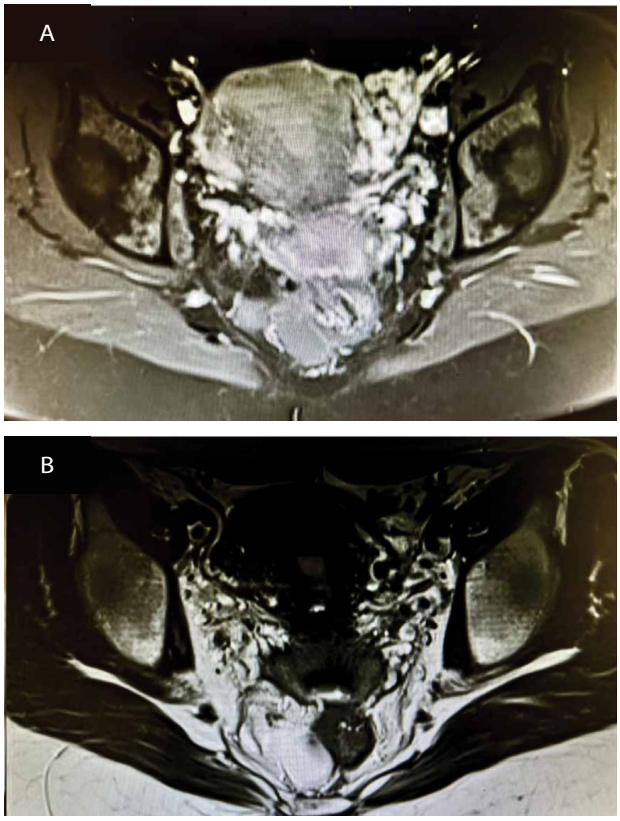

FIGURE 1. A: T1-weighted MRI sequence indicating rectal protrusion below S5 level. B: T2-weighted MRI sequence indicating rectal protrusion below S5 level.

DISCUSSION

Secondary PHs could rarely develop after significant pelvic surgeries, such as APR, extralevator abdominoperineal excision (ELAPE) or pelvic exenteration (PE), typically within 6 months to 5 years postoperatively. After APR, PH requiring repair occurs in less than 1% of cases, compared to approximately 3% after PE [9,10], but the true incidence might be higher due to the non-reported asymptomatic PH. These hernias often arise when only ischiorectal fat and skin remain for perineal, allowing for small bowel herniation.

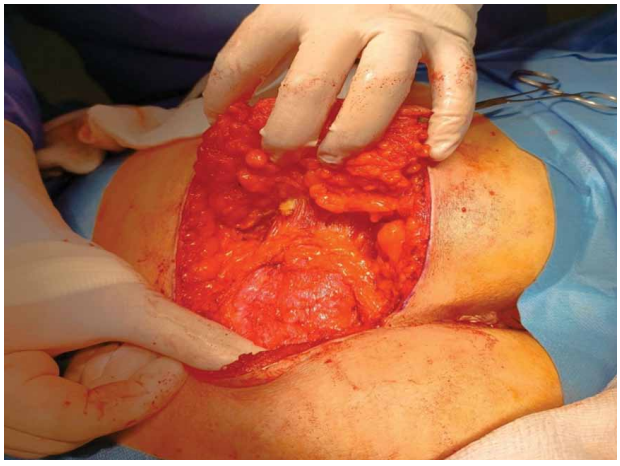

FIGURE 2. Perineal sac with the posterior rectal wall.

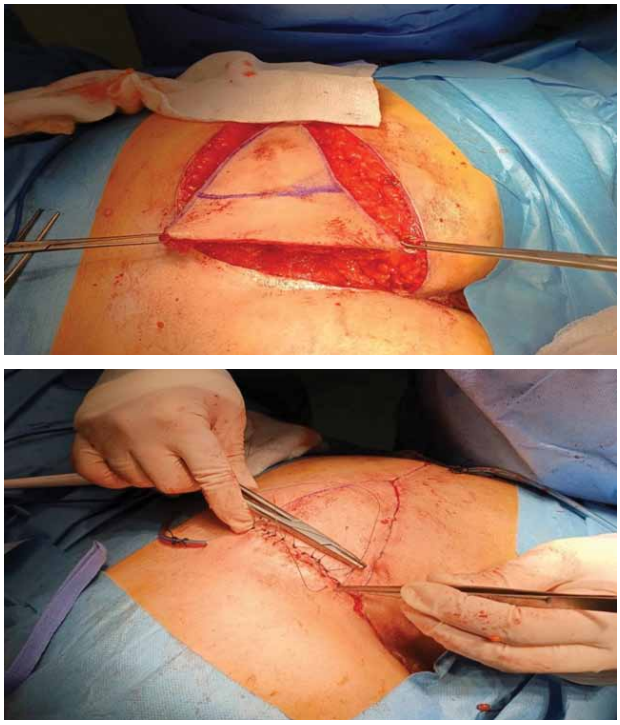

FIGURE 3. A: Flap preparation. B: Flap attachment.

Various other factors contribute to PH formation after surgery, including obesity, smoking, female gender, previous hysterectomy, coccygectomy, pelvic radiation therapy, and perineal wound infection [11-14]. Speculation still exists that the incidence of PH has risen during the last years, due to the advances in rectal cancer treatment with the use of neoadjuvant radiotherapy, which seems to raise the risk of perineal wound complications [10,13]. In our case, a prior pelvic surgery involving the resection of the anococcygeal ligament and partial coccygectomy facilitated the herniation of the rectum into the retrorectal space.

FIGURE 4. Postoperative healing.

While the majority of PHs following APR and PE are asymptomatic and go unnoticed, symptoms may include bulging, discomfort, pain, small bowel obstruction, incarceration or strangulation, and dysuria [2]. Diagnosis can be challenging unless significant signs and symptoms are present, prompting a high index of suspicion, especially in patients with perineal pain. The potential differential diagnosis of PHs encompasses lipomas, rectoceles, fibromas, rectal prolapse, and sciatic hernias. Imaging techniques such as herniagraphy, CT scans, pelvic floor ultrasound, defecography studies and dynamic MRI could establish the diagnosis [15,16].

Surgical repair of a PH is indicated when associated symptoms develop. Other indications include complications like small bowel obstruction and or strangulation, skin breakdown, and evisceration [8]. However, the surgical approach to the hernia defect poses challenges due to the confined pelvic space, the need to reduce and control the bowel, as well as ensuring adequate mesh fixation. Various surgical strategies have been suggested for the management of PH, including diverse approaches (abdominal or perineal or combination of both, open or minimally invasive) and different closure techniques (primary perineal closure, non-absorbable mesh, composite mesh, biological mesh, flap reconstruction) [17-19]. Ongoing research is also focused on PH prevention, exploring the potential benefits of synchronous reconstruction of the pelvic floor following rectal excision [20-22].

Based on the available literature, predominantly of case reports and small case series with limited meta-analyses and systematic reviews, perineal approach has been the preferred method for repair [4,7,8]. This preference is attributed to a broader exposure of the surgical field compared to the abdominal approach, facilitating mesh placement, fixation, and the repair of cutaneous defects. However, the combined abdominoperineal approach has gained popularity during recent years, because it combines the advantages of the perineal approach with the easier mobilization of the herniated contents offered by the abdominal approach. However, morbidity, overall complications and surgical site occurrences (SSO) exhibit significant heterogeneity across studies comparing perineal and abdominal approaches, while recurrence rates appear similar. Regarding the promising combined approach, data is limited and it is premature to draw conclusive insights for its use. Currently, an abdominal approach can be pursued laparoscopically, which maintains the benefit of the abdominal approach with all of the advantages of minimally invasive approaches, also showing a low recurrence rate [23-25].

Concerning the methods of PH repair, there has been

a decline in primary repairs over the past decades, accompanied by a rise in mesh repairs. However, primary repair remains a viable option for patients who do not prefer or present contraindications for mesh implantation [7]. Overtime, there has been a growing utilization of biological mesh, which has been linked to lower infection rates and overall morbidity, and synthetic mesh, which has been associated with decreased recurrence rates. Notably, a recent meta-analysis suggested that the flap method had the lowest recurrence rates, but the limited number of cases treated with this method prevents us from drawing safe and significant conclusions [8]. Another synchronous meta-analysis suggests that there are no significant differences in recurrence between the use of synthetic or biological mesh. However, the addition of a tissue flap to mesh repair may yield favorable outcomes [26].

CONCLUSION

In conclusion, perineal hernias represent a challenging clinical entity, with diverse etiologies and evolving management strategies. Surgical repair remains the primary choice for symptomatic perineal hernias, guided by individual patient characteristics and preferences. The shift towards mesh and perineal repairs underscore the dynamic nature of treatment trends. However, the heterogeneity in outcomes and recurrence rates across different surgical approaches warrants careful consideration in selecting the most appropriate strategy. In essence, perineal hernias demand a nuanced and multidisciplinary approach, reflecting the evolving landscape of surgical interventions and highlighting the need for ongoing investigation to enhance our understanding and management of this complex condition. The present case study sheds light on the intricacies of diagnosing and treating a posterior perineal hernia, emphasizing the importance of tailored interventions based on associated symptoms and complications.

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REFERENCES

1. Kann BR. Perineal hernias. J Long Term Eff Med Implants. 2010;20(2):149-57.
2. Stamatiou D, Skandalakis JE, Skandalakis LJ, Mirilas P. Perineal hernia: Surgical anatomy, embryology, and technique of repair. Am Surg. 2010 May;76(5):474-9.
3. Cali RL, Pitsch RM, Blatchford GJ, Thorson A, Christensen MA. Rare pelvic floor hernias. Report of a case and review of the literature. Dis Colon Rectum. 1992 Jun;35(6):604-12.
4. Balla A, Batista Rodríguez G, Buonomo N, Martinez C, Hernández P, Bollo J, et al. Perineal hernia repair after abdominoperineal excision or extralevator abdominoperineal excision: A systematic review of the literature. Tech Coloproctol. 2017 May;21(5):329-36.
5. Salati SA, Arkoubi AY. Perineal hernia after abdominoperineal resection - a systematic review. Pol Przegl Chir. 2022 Apr;94(6):61-70.
6. Bertrand K, Lefevre JH, Creavin B, Luong M, Debove C, Voron T, et al. The management of perineal hernia following abdomino-perineal excision for cancer. Hernia. 2020 Apr;24(2):279-86.
7. Maspero M, Heilman J, Otero Piñeiro A, Steele SR, Hull TL. Techniques of perineal hernia repair: A systematic review and meta-analysis. Surgery. 2023 Feb;173(2):312-21.
8. Junsheng Li, Lisheng Wu, Xiangyu Shao, Tao Cheng. Postoperative perineal hernia repair: What is the evidence? Surg Today. 2023 Oct;53(10):1105-15.
9. Levic K, Kasper von Rosen, Orhan Bulut. Thue Bisgaard. Low incidence of perineal hernia repair after abdominoperineal resection for rectal cancer. Dan Med J. 2017 Jul;64(7):A5383.
10. McKenna NP, Habermann EB, Larson DW, Kelley SR, Mathis KL. A 25 year experience of perineal hernia repair. Hernia. 2020 Apr;24(2):273-8.
11. Aboian E, Winter DC, Metcalf DR, Wolff BG. Perineal hernia after proctectomy: Prevalence, risks, and management. Dis Colon Rectum. 2006 Oct;49(10):1564-8.
12. Martijnse IS, Holman F, Nieuwenhuijzen GAP, Rutten HJT, Nienhuijs SW. Perineal hernia repair after abdominoperineal rectal excision. Dis Colon Rectum. 2012 Jan;55(1):90-5.
13. Mjoli M, Sloothaak DAM, Buskens CJ, Bemelman WA, Tanis PJ. Perineal hernia repair after abdominoperineal resection: A pooled analysis. Colorectal Dis. 2012 Jul;14(7):e400-6.
14. Zimmer S, Fendrich V, Heverhagen J, Rothmund M. Perineal hernia. A rare complication following abdominoperineal rectal amputation. Chirurg. 2009 May;80(5):462, 464-5.
15. Ikuo Watanobe, Shozo Miyano, Michio Machida, Hiroyuki Sugo. Primary anterior perineal hernia: A case report and review of the literature. Asian J Endosc Surg. 2020 Oct;13(4):600-4.
16. Morales-Cruz MA-O, Oliveira-Cunha M, Chaudhri S. Perineal hernia repair after abdominoperineal rectal excision with prosthetic mesh-a single surgeon experience. Colorectal Dis. 2021 Jun;23(6):1569-72.
17. Mojadeddi ZA-O, Harmankaya S, Öberg S, Rosenberg J. Surgical technique for primary perineal hernia repair: A systematic scoping review. Hernia. 2023 Aug;27(4):751-63.
18. Narang SK, Alam NN, Köckerling F, Daniels IR, Smart NJ. Repair of perineal hernia following abdominoperineal excision with biological mesh: A Systematic Review. Front Surg. 2016 Sep;3:49.
19. Wolthuis AM. Mesh, flap or combined repair of perineal hernia after abdominoperineal resection - A systematic review and meta-analysis. Colorectal Dis. 2022 Nov;24(11):1270-1.
20. Musters GD, Klaver CEL, Bosker RJI, Burger JWA, Van

Duijvendijk P, Van Etten B, et al. Biological Mesh Closure of the Pelvic Floor After Extralevator Abdominoperineal Resection for Rectal Cancer: A Multicenter Randomized Controlled Trial (the BIOPEX-study). Ann Surg. 2017 Jun;265(6):1074-81.
21. Foster JD, Pathak S, Smart NJ, Branagan G, Longman RJ, Thomas MG, et al. Reconstruction of the perineum following extralevator abdominoperineal excision for carcinoma of the lower rectum: A systematic review. Colorectal Dis. 2012 Sep;14(9):1052-9.
22. Buscail E, Canivet C, Shourick J, Chantalat E, Carrere N, Duffas J-P, et al. Perineal wound closure following abdominoperineal resection and pelvic exenteration for cancer: A Systematic Review and Meta-Analysis. Cancers (Basel) 2021 Feb;13(4):721.
23. Goedhart-de Haan AMS, Langenhoff BS, Petersen D, Verheijen PM. Laparoscopic repair of perineal hernia after abdominoperineal excision. Hernia. 2016 Oct;20(5):741-6.
24. Rayhanabad J, Sassani P, Abbas MA. Laparoscopic repair of perineal hernia. JSLS. 2009 Apr-Jun;13(2):237-41.
25. Ghellai AM, Islam S, Stoker ME. Laparoscopic repair of postoperative perineal hernia. Surg Laparosc Endosc Percutan Tech. 2002 Apr;12(2):119-21.
26. Sharabiany S, Brouwer TPA, Kreisel SI, Musters GD, Blok RD, Hompes R, et al. Mesh, flap or combined repair of perineal hernia after abdominoperineal resection - A systematic review and meta-analysis. Colorectal Dis. 2022 Nov;24(11):1285-94.

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Book Chapter

Brown J, Murphy KH. Adult-onset Still's disease. In: Maddison PJ, Woo P, Glass DN, Eds. Oxford Textbook of Rheumatology, 3rd ed. Oxford, UK: Medical Publication, 2010. Pp. 1127–31.

Book

Smith MD. Introduction to Gynaecology, 6th ed. New York, USA: Institutional Press, 2005. P. 15.

Report

World Health Organization. Issues in Health Services Delivery. Ge-

neva, Switzerland: World Health Organization. WHO/EIP/00l. Pp. 3–4.

Thesis

Rowe L. DNA damage-induced reactive oxygen species: A genotoxic stress response. PhD Thesis, 2012, Emory University, Georgia, USA. Pp. 315–22.

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Smith AD. Pregnancy after 35. From: www.marchof-dimes.com/pregnancy Accessed: Sep 2016.

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