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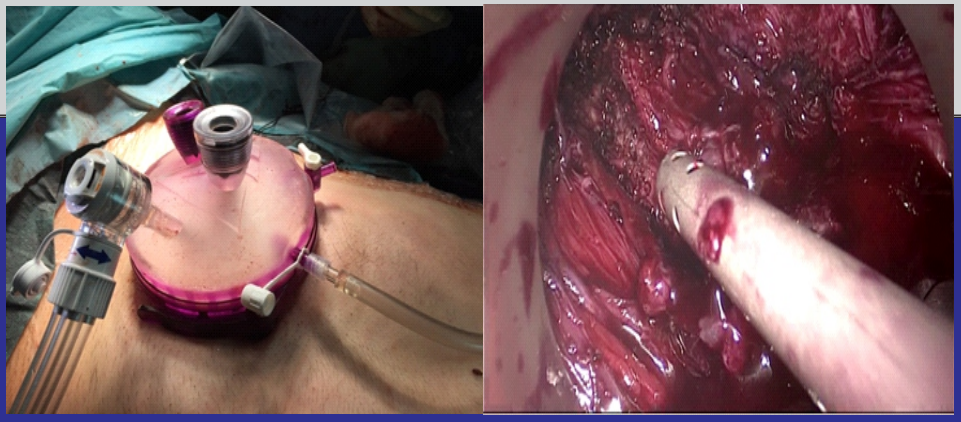

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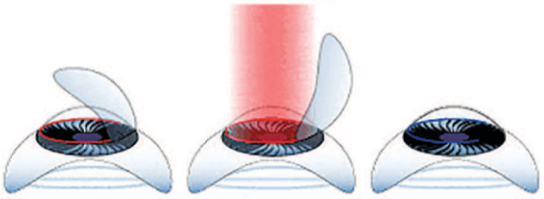

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LEADING ARTICLE

Global trends and equitable care in endocrine surgery

Ranil Fernando
North Colombo Teaching Hospital, Ragama, Sri Lanka

Key words: Equitable care; endocrine surgery;

Introduction

The responsibility of surgeons is to offer the best possible care for the patients. In the era of information technology newer techniques are being introduced every day. Nothing causes dramatic change as the introduction of a revolutionary technology. The newer techniques tend to be expensive and the cost factor creates problems with availability & equity. What is new may not always be the best. Conflicts between what is available and what is possible arise. The cardinal principle in medicine is that all patients must receive the best possible care irrespective of any other consideration. This is the principle of "Equitable Health Care". In equitable health care, coverage should be universal; be available to most (if not all), should be continuous and should be affordable to individuals and families. Balancing the possibility and availability equation is a difficult task for health systems. If one were to take an objective view of Global Surgical Care, it becomes apparent that, while on the one hand tremendous improvements have been made in technology and it's applications in surgery, most people worldwide though needing a surgery will not receive it. Nor are they likely to see a trained surgeon. This is the number one surgical problem in the world [1].

This stark reality must temper our choices when decisions are made in recommending options in surgery. The ensuing account deals with this in relation to endocrine surgery. The Disease Burden in Endocrine surgery Management of thyroid disease remains the main workload in endocrine surgery (80-90%) world over. Goitre remains a problem in most parts of the world especially the low and middle income groups and according to the WHO 15.8% of the world population is likely to be affected by Goitre [2]. There appears to be an increase in the prevalence of thyroid cancer in certain parts of the world [3, 4, 5]. Benign and malignant thyroid disease will be the major burden in endocrine surgery everywhere in the world. Parathyroid disease and adrenal disorders form the rest of the burden while islet cell disorders of the pancreas and other endocrine surgical disorders are rare disease except in specialized referral centres. While being cognizant of the latest developments and trends in thyroid, parathyroid and adrenal surgery, care is needed when recommendations are made in their investigations and treatment, as the small health care budgets in low and middle income countries are likely to cause significant problems with equity of care. The newer methods are costly, and thus there is a potential for reduced availability worldwide.

Global trends and a historical perspective of endocrine surgery

In the early part of 20th century, pioneering efforts of several surgeons made endocrine surgical procedures, low risk operations.

Thyroidectomy is a very safe surgical procedure with extremely low complication rates quoted by centres with large patient numbers e.g. hypoparathyroidism of less than 2%, injury to recurrent laryngeal nerve 1%, mortality less than 1%. The surgical incisions and operative techniques have changed very little during this time. Currently, utilizing 3-6 cm collar incisions, modern day surgeons carry out thyroidectomies safely. Standard open thyroidectomy (ST) remains the benchmark in the management of benign and malignant thyroid disease.

The era of endoscopic surgery has come of age now and minimally invasive thyroid surgery is here to stay. Robotics, telesurgery, Lasers, surgical simulators and other advanced technologies are in use in several parts of the world. This raises many new problems for surgeons and decision makers. Is it better to have a PET scanner or to provide access to basic investigations for most? Is endoscopic surgery the best for all types of endocrine surgery? What about cost effectiveness and what about evidence? Is endoscopic surgery justified in parathyroid surgery? Or is it a "market driven exercise" solely aimed at promoting a "minimally invasive parathyroid surgery and an attempt at increasing number of referrals for parathyroid surgery [6]. These questions need answers. The cost effectiveness of endoscopic parathyroidectomy is not established. Less expensive alternatives such as open mini incision parathyroidectomy may be a better alternative [6].

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In terms of evidence, lack of solid evidence in endocrine surgery is one of the main draw backs encountered in many areas of management. At best it is based on experiences of high volume centres with a few randomized trials to support practice. The decision making then becomes difficult and may be tempered and guided by the individual preference of a surgeon. A good example is the use of robotics in thyroid surgery. While robotic thyroidectomy may be called 'minimally invasive', it clearly is not minimally invasive. The approach to the thyroid from a remote access causes a lot of tissue damage not encountered in the open method. In terms of cost, it has been shown that, even in a high income country like USA it is not likely to be available to most people due to its high cost. It may survive as niche operations [7]. In terms of safety, small number of studies, lack of randomization of clinical trials involving this approach leaves many questions unanswered.

Further research, especially in areas of cost benefit analysis and controlled trials with larger numbers, is required to assess the outcome, patient satisfaction, and cost benefit of this surgery [8, 9]. While newer techniques must be learnt and practiced, the surgeon must be aware of the issues involved and must not lose sight of equitable care based on best available current evidence.

The main issues that need to be addressed in providing equitable care in endocrine surgery

There are many unanswered questions that need to be considered in providing equitable care in endocrine surgery. They are summarized as follows;

What do we offer our patients?
Do we favour our special interest?
Do we over sell the newer techniques?
Is the industry putting pressure to use certain devices?
Are the decisions based on solid evidence?
How do we attempt to provide equitable care?

Collaborative surgical research may be one method to provide this equity. Every year more than 200 million surgical operations are carried out worldwide [10]. In addition there are other areas that need to be clarified. What do we recommend to the Health System? Each country must decide for itself and the surgeons must recommend to the health care system. Development of guidelines will assist in this. How do we train the postgraduates? Most of them are likely to practice in non-specialized centres. They should able to practice with limited facilities, yet provide good endocrine surgical service. They must undoubtedly be taught the newer techniques. Trainers must be cognizant of steeper learning curve for newer procedures. Open methods need to be learnt by all .What is old is not always bad. Obituary of the open procedures is not due yet. When we are in trouble we always 'open up'. Role of the endoscope in thyroid parathyroid surgery needs irrefutable evidence. In the diseases of the adrenal and endocrine pancreas, endoscopic surgery makes 'sense' as the tissue injury is minimized.

Concluding remarks

Providing equitable care is the responsibility of all heath care providers and individual surgeons. Technological advances offer alternatives in providing the best medical care for patients. These advances need to be weighed in the balance against their costs. Then only the benefits of these technological advances be accurately calculated against the overall societal cost. The burden that these technological advances place on limited resources is a consideration that surgeons need to bear in mind in making surgical choices. Equitable care in endocrine surgery can then be provided to most within the frame work of emerging global trends if evidence, wisdom and honesty are the guiding principles.

All authors disclose no conflict of interest. The study was conducted in accordance with the ethical standards of the relevant institutional or national ethics committee and the Helsinki Declaration of 1975, as revised in 2000.

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SCIENTIFIC ARTICLE

Transanal total mesorectal excision (TaTME) for inflammatory bowel disease (IBD): review of technique and initial experience

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Key words: Trans anal surgery; TaTME; inflammatory bowel disease; pouch surgery

Abstract

Introduction

Trans anal minimal invasive surgery (TAMIS) is a novel technique gaining popularity in colorectal surgery due to its precision in pelvic dissection and easy accessibility to the distal rectum. Its use in colorectal cancer surgery is well documented although inflammatory bowel disease (IBD) poses a unique set of disease-specific and procedure-related challenges. Unlike in cancer surgery, the wide disease spectrum with varying morphological changes in IBD would require the surgeon to adapt accordingly from port insertion to wound closure. This article describes our experience with the first 60 procedures.

Methodology

Patients affected by IBD requiring proctectomy with or without total colectomy from 2013 to 2016 were offered Trans anal total mesorectal excision (TaTME) on a TAMIS and Single Incision Laparoscopy (SILS) combined platform. Airseal ® insufflation on GelpointPath ® platform with monopolar diathermy was used for rectal surgery. A second team using ultrasonic dissection carried out concomitant abdominal dissection. Procedural modifications were adopted based on authors' personal experience. Standard ileoanal S pouch with stapler anastomosis was performed. Surgical time, blood loss and patient demographics were recorded.

Results

All 60 patients (male – 44; median age 42.5; range 19-75) presented during the study period underwent TaTME for the rectal dissection with an 8% conversion rate. Of the total 38 (63%) were done for ulcerative colitis and the perineal phase has taken a median time of 141.8 minutes. Ileo-anal pouch surgery was performed in 27 (45%) patients. Two patients (3.3%) required re-intervention due to complications in the abdominal procedure. Two patients required vacuum dressing for wound closure.

Conclusion

TaTME is a safe and feasible procedure in IBD surgery. Specific difficulties due to the inflammatory process which results in difficult dissection can be overcome with attention to anatomical details and the use of specific instruments.

Introduction

Total mesorectal excision (TME) with trans anal minimal invasive surgery (TAMIS) was developed on the platform of transanal endoscopic microsurgery (TEM) described by Buess and colleagues [1]. It is believed that quality of the rectal cancer specimens can be improved and the challenges faced during deep pelvic dissection can be overcome through this 'bottom-up' technique. The transanal procedure is combined with either laparoscopic or single incision laparoscopic approach from the abdomen. Atallah et al published the first series of TAMIS-TME in 20 patients with rectal cancer [2]. Although evidence on the efficacy of TAMIS-TME in rectal cancer has been accumulating [3, 4]. there is scarce data on its use in inflammatory bowel disease. Completion proctectomy due to intractable perineal disease or proctectomy with ileoanal pouch creation in suitable patients are the two most common procedures performed in this setting. Although completeness of circumferential resection margin is not mandatory in benign disease, there are unique issues pertaining to patients with inflammatory bowel disease (IBD) in the peri-operative period during rectal surgery. IBD encompasses ulcerative colitis (UC), Crohn's disease (CD) and indeterminate colitis in a small proportion of patients. Effects of chronic inflammation obscure the anatomical planes making dissection difficult and also affect the postoperative wound management. Use of specific instruments and devices can help in improving surgical outcome. In this article, we aim to describe the specific issues related to performing Transanal rectal excision (TaTME) in the setting of IBD and the initial learning experience from the first 60 cases performed at the St. Mark's Hospital, London.

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Difficult phases and methods to overcome them are described based on the authors' personal experience.

Methodology

Platform

There are many platforms used for transanal surgery such as Transanal endoscopic operation (TEO®) proctoscope (KarlStorz, Tuttlingen, Germany), Endorec Trocar (Aspide Medical), GelPOINTPath® Transanal Access Platform (Applied Medical, Rancho Santa Margarita, CA). We prefer the GelpointPath® port with a flexible sleeve and a gel port for port insertion [1]. This port has the advantage of increased freedom of movement [5]. GelpointPath® also provides freedom to select different port insertion sites depending on preference. The authors believe that port selection should be based on individual preference and experience.

Port insertion and purse string

The transanal phase may be performed concomitantly with the abdominal phase or in tandem either before or after. We prefer to perform the two procedures concomitantly using the single incision laparoscopy (SILS) port (Figure 2). The anal canal is accessed using a Lone Star retractor® (Lone Star Medical Products Inc., Houston, Texas, USA). For restorative procedures we use a clear anoscope to facilitate placing the purse-string suture (2/0 polypropylene) 2 cm above the dentate line. This allows direct visualisation of the dentate line and the exact location of the rectotomy to ensure that excess inflamed mucosa is not left behind. Dissection is initiated distal to the purse-string prior to insertion of the port under direct vision and the TME plane is entered. This step can also be performed after inserting the transanal port. For proctectomy without restoration, the purse- string is applied at the anal verge and the dissection is initiated in the inter-spinchteric plane.

Figure 1. The arrangement of the transanal port for the trans anal dissection. The anal canal is being retracted with a 'Lonestar' retractor and the 'GelpointPath port inserted with two working ports and an 'Air-Seal' insufflation port.

Insufflation

Our initial experience was with the standard CO2 insufflator, although the smoke generated obscured vision. In the last 40 cases we have been using the Surgiquest Airseal® (Alder Instrument Company, Atlanta, GA, USA) device for insufflation and this provides well controlled insufflation pressure with continuous circulation preventing smoke accumulation. A specially designed Airseal® trocar is required for this and our preference is to use the 5mm version (Figure 1). As the tissue planes are not well defined in the presence of inflammation, devices to reduce residual smoke and improve vision greatly facilitates dissection.

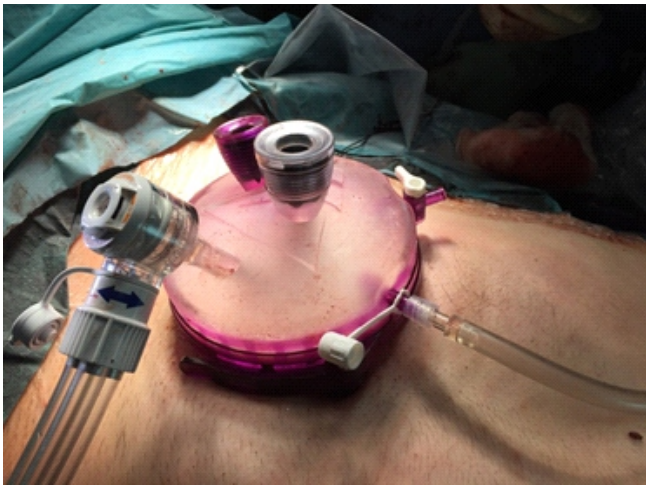

Figure 2. The arrangement for the abdominal dissection with Single Incision Laparoscopy port (SILS).

Figure 3. Severe perineal Crohn's disease with destruction of the perianal skin.

Endopelvic fascia

The endopelvic fascia is a thickened connective tissue layer that covers the pelvic floor musculature. Once the dissection reaches the level of the anorectal junction, it is necessary to cut through the endopelvic fascia. The best site to perform this step is at 7 or 8 o' clock positions. Anteriorly the pelvic floor is not well defined and posteriorly at 6'o clock the fascia forms a midline raphe, which makes dissection at these points difficult. This step is pertinent to continue the dissection in the correct plane which will otherwise tend to sway laterally and result in dissection deep to the pelvic fascia. It should be borne in mind that dissection deep to the fascia will result in troublesome bleeding.

Anastomosis in restorative procedures

The majority of UC patients undergo restorative procedures with an ileal pouch. The small bowel is extracted through the SILS port site at the RIF and the pouch formed extra-corporeally. We carry out the double purse-sting technique of ileal pouch-anal anastomosis. The ileal J pouch is constructed in the standard manner using linear staplers and the anvil of the circular stapler (Chex® CS, Frankeman International, Hong Kong) secured with a No 2/0 polypropylene suture. This stapling device has a long anvil coupled with a rod and allows easier withdrawal from the anus when compared with other circular staplers. We use the Lone Star® retractor with the transparent anoscope to visualize the resection margin above the dentate. The distal purse-string is then placed trans-anally using a 2-0 polypropylene suture. This is not secured initially.

After completing the purse string, the pouch is guided in to the pelvis laparoscopically and the anvil is grasped with a Robert's forcep inserted through the distal purse string. Once the shaft of the anvil is pulled, through the purse-string and fixed to the spike of the circular stapler.

Subsequently the circular stapler is closed and fired after confirming the orientation of the pouch with the abdominal team. It is important to make sure the small bowel mesentery is not twisted along its axis, prior to performing the anastomosis.

Perineal wound in non- restorative procedures

The perineal wound poses a formidable challenge especially in Crohn's disease. Involvement of the perineum by fistulating disease makes it necessary to excise a significant area of perineal soft tissue, which can leave a large defect. Due to its inflamed and infected nature, primary closure is not taken up in these complicated cases. Usually we apply a vacuum dressing primarily and re-assess the wound in 4 to 6 weeks' time to decide on a flap closure with the plastic surgeons.

Table 1. Patient demographics of the first 60 cases- TaTME in IBD

Cases	**N = 60**
UC	38 (63%)
CD	22 (37%)
Age (median years: range)	42.5 (19-75
Sex	
Male	44 (73%)
Female	16 (27%)
ASA	
I	14
II	43
III	03
BMI (median: range)	25.4 (20.9 – 30.6)

Results

Sixty consecutive patients requiring proctectomy with or without restoration for CD and UC underwent the procedure at the unit up to July 2016. None of the patients were excluded, even in the presence of areas of perineal breakdown secondary to Crohn's disease. The median age of the patient population was 42.5 years (range 19 to 75 years) and 44 (73 %) were male. Restorative procedures with ileo-anal pouch creation were performed in 27 (45%) of the patients (Table 1). Four patients (6.7%) had colorectal cancer diagnosed in the specimen following surgery. Average surgical time taken for the transanal phase was 141.8 minutes with an 8% (n=5) conversion rate, the majority (n=3) due to the dissection plane being obscured by inflammation. Two patients out of the 60 (3.33%) required a vacuum dressing for the perineal wound management. Eight post-operative complications were experienced (Clavien-Dindo 1:4, 2:2, 3; 2). The two complications requiring re-intervention were bowel obstruction due to twisting of the mesentery and a tight ileostomy.

Discussion

Inflammatory bowel disease poses a unique series of challenges for the trans-anal approach compared to malignant disease. Severe perineal Crohn's disease may present as completely deformed anal opening (Figure 3) and with a strictured anus. However, these are not contraindications to the trans-anal approach.

The initial plane of dissection in these cases needs to be placed further away from the anal verge to encompass the diseased perineal skin and subcutaneous tissue of the perineum in the specimen. A major challenge during rectal dissection in IBD is the inflammation obscuring tissue planes (Figure 4). Although extramural inflammation is expected in CD, our experience is that it also affects UC. In patients with long standing active UC, the TME plane is as challenging as in CD. The mesorectal fat is more friable and may bleed easily.

Figure 4. Dissection planes obscured by bleeding due to inflamed tissue planes. The diathermy coupled with suction device increases efficiency due to not having to change instruments.

The ENDOPATH Electrosurgery Probe Plus® (Ethicon Endo-Surgery, Johnson & Johnson, Germany) monopolar diathermy device we use is equipped with an inbuilt suction mechanism which is very useful during intraoperative bleeding (Figure 6). Authors also use 'tonsillar swabs' to apply pressure and use the same to apply upward traction on the rectum. One specific site of troublesome bleeding is the middle rectal artery, which can be well defined, especially on the left side and would require clipping before division. Recognition of opening in to deeper lateral planes is helped by the 'Halo' sign described by Bernardi et al [6]. They described the appearance of an 'O' shape defect when a new fascial plane is opened. However, this is not an absolute sign but should alert the operator to re-evaluate. Another well recognized challenge during dissection is the anterior prostatic plane in UC patients [6]. This area anyway poses a challenge due to the close proximity of the urethra and prostate to the rectum, although in this particular group of patients the plane was heavily fibrotic. This is an interesting observation, as UC is not expected to cause trans-mural inflammation. Concurrent abdominal dissection is helpful in guiding the two dissection planes to meet each other. Results from TaTME in benign disease is lacking in comparison to its use in malignant disease.

A recent report by de Buck van Overstraeten demonstrated a comparable complication rate and lesser postoperative morbidity in TaTME with IPAA compared to conventional laparoscopic pouch surgery [7]. Comparing 97 TaTME procedures with 119 trans-abdominal procedures, they reported a significantly lower complication rate and a lower comprehensive complication index (CCI) in the TaTME group. Although IBD is a benign disease, the authors tend to carry out dissection in the TME plane for several reasons. The current patient cohort had an incidental cancer detection rate of 7% in the dissected specimens. The field change in the colorectal mucosa that occurs with inflammation, predisposes to dysplasia and cancer that may go undetected in focused biopsies. Carrying out a close dissection technique could compromise the oncological safety in this group of patients. Also, a yet unproven theory suggests the perirectal or peri colic fat in Crohn's disease contributes to the inflammation. Lindsey and colleagues have observed no difference in the rates of sexual dysfunction following either technique in IBD [8]. Therefore, the authors feel that the argument for a close rectal dissection lacks support. Patients with perineal Crohn's who undergo completion proctectomy, pose a challenges in the management of the perineal wound. Defects following excision in infected fields are managed with vacuum dressings followed by a flap cover (Figure 5). Surprisingly, some of these large defects contract and granulate significantly, not requiring a flap cover (Figure 6). Uncomplicated wounds in the perineum are closed in layers vertically with an abdominal drain placed in the pelvis.

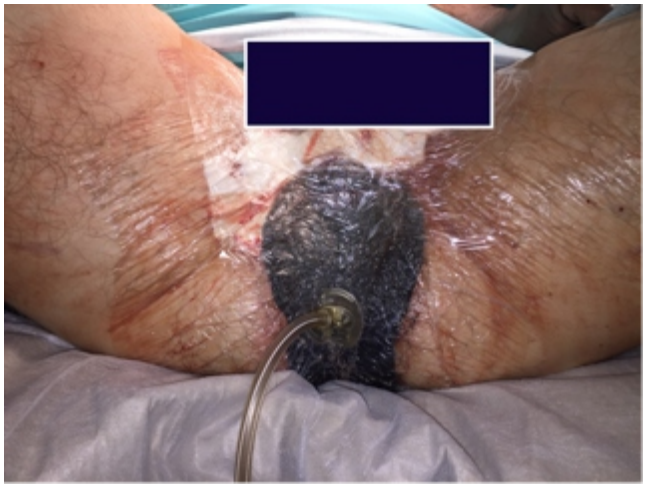

Figure 5. Vacuum dressing applied to a perineal defect in a ptient with Crohn's disease following TaTME.

Figure 6. Wound constricted 6 weeks after the application of vacuum dressing.

A common complication to look out for in the immediate postoperative period is wound breakdown, although caution in decision-making as to which wounds can be closed primarily could prevent this. Some of these wounds which fail, might result in a chronic discharging sinus [9]. Another complication related to completion proctectomy in CD patients, is a pelvic collection [10]. These collections may be managed conservatively or with intervention in the form of radiological guided aspiration, depending on the size and the sinuses with the use of video assisted anal fistula treatment (VAAFT) technique. Accumulation of more outcome data on this relatively novel technique, will allow the surgeons to evaluate its advantages and disadvantages over conventional trans-abdominal surgery.

Conclusion

In this article we describe the techniques and challenges related to transanal resection for inflammatory bowel disease. We have demonstrated that TaTME is technically feasible in IBD and offers some advantages over standard laparoscopy, especially in relation to allowing control of the point of rectotomy and anastomosis. Post-operative wound management following trans anal surgery in this cohort of patients is at times challenging, although the results may be favourable in the long term.

All authors disclose no conflict of interest. The study was conducted in accordance with the ethical standards of the relevant institutional or national ethics committee and the Helsinki Declaration of 1975, as revised in 2000.

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SCIENTIFIC ARTICLE

Post-operative outcome following ileal pouch-anal anastomosis (IPAA)

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Key words: Post-operative; ileal pouch; anal; anastomosis

Abstract

Introduction

The ileal pouch-anal anastomosis (IPPA) procedure is the surgery of choice in severe ulcerative colitis (UC) and familial adenomatous polyposis (FAP). The objectives of the study were to assess symptomatic improvement, complications, effect on sexual function and quality of life (QOL) following IPAA procedure.

Methods

Twenty one patients who underwent IPAA procedure at a tertiary care unit with a minimum of one year follow-up from 2009, were included. QOL was assessed retrospectively prior to surgery and one year after surgery using Cleveland Global Quality of Life Score (CGQLS). Details of pre and post-op symptoms, complications and sexual function were obtained using clinical records, operative notes and interviewer administered questionnaire.

Results

Male: female ratio was 1.33:1. Fourteen (66.7%) were sexually active and seven (33.3%) were not. Mean age was 40.48(range, 17-69) years. 13(61.9%) had UC and 8(38.1%) had FAP. Mean pre-op CGQL scores for UC and FAP were 0.5754 and 0.7537 respectively. Post-op CGQLS for UC and FAP were 0.7532 and 0.7070. There was no statistically significant difference between CGQL scores against the indication for surgery (P=0.779). Stool frequency was significantly reduced in UC (pre-op=12.4, post-op=5.2 per day, p=0.004) but no difference in FAP (pre-op=2.6, post-op=3.5 per day, p=0.292). Post-operatively, one patient developed erectile dysfunction and another patient developed dyspareunia.

Conclusion

There is no significant difference of CGQL scores following IPAA procedure in relation to the surgical indication. IPAA significantly reduced stool frequency per day in UC but not in FAP. Erectile dysfunction and dyspareunia are possible sexual dysfunctions following IPAA procedure

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Introduction

Ulcerative colitis (UC) is a chronic inflammatory bowel disease which involves colon and rectum. Familial adenomatous polyposis (FAP) is an autosomal dominantly inherited disease which leads to adenomatous polyps in large numbers throughout the colon. Both conditions are associated with colorectal cancer whereas, the latter has 100 percent risk of cancer if left untreated.

Ileal pouch-anal anastomosis procedure (IPAA) is the surgery of choice in UC and FAP. In 1978 Parks et al [1] reported four cases undergoing IPAA successfully. Advantages of IPAA include, avoiding a stoma, cosmetically acceptable for the patient and mimics the natural bowel function. Improving quality of life following surgery for UC and FAP is a major part of the management.

Objectives

- To determine the symptomatic improvement following IPAA
- Describe the pattern of complications following IPAA
- Assess the impact of complications on quality of life
- To study the effect on sexual function following IPAA
- To study the difference of quality of life (QOL) according to the indication for the ileal pouch-anal anastomosis procedure

Methods

Cross sectional descriptive and analytical retrospective study design was adopted. The study was conducted in the Professorial Surgical Unit, National Hospital of Sri Lanka (NHSL) on patients who underwent IPAA procedure from April 2009 to May 2016. Patients who underwent IPAA, with a minimum follow up period of one year were included in the study. Patients with psychiatric conditions and other conditions which can affect the quality of life considerably (i.e. malignancies, diabetes mellitus, osteoarthritis,

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rheumatoid arthritis etc.) were excluded from the study. Ethics clearance was obtained from ethics review committee of the National Hospital Sri Lanka. Informed written consent from patients to participate in the research was obtained prior to the interview.

Interviewer administered questionnaire was administered according to their preferable language. The interviewers were uniformly trained regarding the administration of the questionnaire. Basic socioeconomic details were obtained from the patients. Additionally, clinic records and operative notes of the participants were reviewed. Sexual dysfunction was assessed by taking a detailed sexual history in a privacy secured clinic room comparing sexual function pre-operatively and one year after surgery.

Pre and post-operative symptoms were assessed using clinical history, clinic records and operative notes. Stool frequency per day, per rectal bleeding, loss of appetite and extra gastro intestinal symptoms like fever, joint pain, red eye, back pain with immobility were assessed pre-operatively and one year after IPAA.

Cleveland Global Quality of Life Score (CGQLS) validated in 1999 by Fazio et al [2] was used to assess the quality of life following Ileal pouch-anal anastomosis procedure. CGQLS consists of 3 components. They are current quality of life, current quality of health and current energy respectively. Each component is given marks out of 10 and average CGQL score is calculated.

The enrolled patients were educated on the CGQLS assessment tool. Subsequently, they were asked to mark the three components of CGQL score in two separate scales recalling the quality of life prior to surgery and one year after surgery.

The questionnaire assessed the details given below.

a) Gender and socioeconomic details
b) Year and the indication of the surgery
c) Cleveland Global Quality of Life assessment tool
d) Symptom assessment
e) Post-operative complications assessment
f) Assessment of the sexual function

Results

Twenty one patients were incorporated into the study. Male: Female ratio was 1.33:1. Thirteen patients (61.9%) had UC and eight (38.1%) had FAP. Mean age was 40.48 (range, 17 to 69) years.

Mean pre-operative CGQL score of all 21 patients was 0.6433. One year after surgery, mean CGQL score was 0.7365.

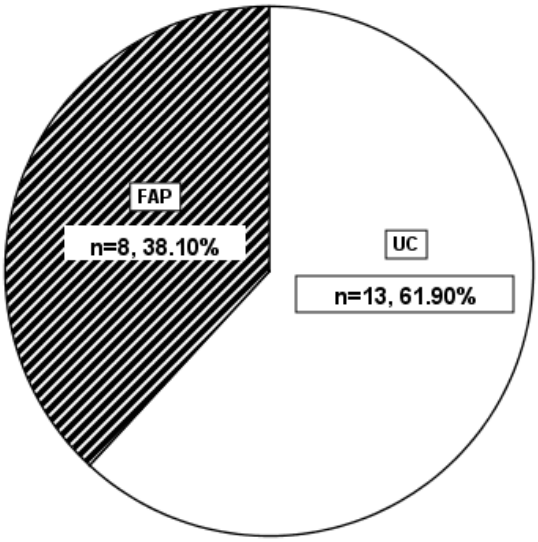

Figure 1. Indication for surgery

Statistical analysis

Post-operative CGQL scores were compared against the indication for surgery after controlling the effect of pre-operative CGQL score using analysis of covariance (ANCOVA) test. There was no statistically significant effect of surgical indication on post-operative CGQL scores after controlling for the effect of pre-operative CGQL scores (p=0.779).

Commonest pre-operative symptom encountered was per rectal bleeding which was present in 20 (95.2%) patients. Twelve (57.1%) patients had loss of appetite prior to surgery. Twelve (92.3%) out of 13 patients with UC had extra gastrointestinal symptoms pre-operatively. Arthralgia was present in 9 (69.2%) patients. 7 (53.8%) had fever pre-operatively. Red eye suggestive of uveitis and severe back pain with reduced mobility suggestive of ankylosing spondylitis were found in 2 (15.4%) patients each.

Symptoms were assessed one year after surgery. Per rectal bleeding persisted in 2 (9.5%) patients, one from the UC group and the other from the FAP group. 3 (14.3%) patients had loss of appetite one year after surgery. Five (38.4%) out of 13 patients with UC had extra gastrointestinal symptoms one year following IPAA. Arthralgia was present in 3 (23.1%) patients one year after surgery. No patients had fever after one year of surgery. Red eye suggestive of uveitis was not found. Severe back pain with reduced mobility suggestive of ankylosing spondylitis was found in 2 (15.4%) patients.

Table 1. Symptom assessment

	Pre-operative	One year following IPAA
Per rectal bleeding	20 (95.2%)	2 (9.5%)
Loss of appetite	12 (57.1%)	3 (14.3%)

Table 2. Extra gastrointestinal symptom assessment

	Pre-operative	One year following IPAA
Extra gastrointestinal symptoms	12 (92.3%)	5 (38.4%)
Arthralgia	9 (69.2%)	3 (23.1%)
Fever	7 (53.8%)	0
Red eye (Uveitis)	2 (15.4%)	0
Severe back pain (Ankylosing spondylitis)	2 (15.4%)	2 (15.4%)

Mean pre-operative stool frequency per day was 12.4 in the UC group. One year after surgery, it reduced to 5.2 per day one year after surgery. In FAP group, mean pre-operative stool frequency per day was 2.6. One year after surgery, it had increased to 3.5 per day.

Wilcoxon signed rank test was used to analyse the pre-operative and one year post-operative mean stool frequencies per day in UC and FAP groups separately.

Among patients with UC, there was a statistically significant reduction in post-operative stool frequency per day compared to pre-operative stool frequency per day ($p=0.004$).

Among patients with FAP, there was no statistically significant difference in post-operative stool frequency per day compared to pre-operative stool frequency per day ($p=0.292$).

Table 3. Complications

	Ulcerative colitis	Familial adenomatous polyposis
Abdominal wound infection	4 (19%)	5 (23.8%)
Anaemia	4 (19%)	3 (14.3)
Pelvic abscess	1 (4.8%)	1 (4.8%)
Incisional hernia	1 (4.8%)	1 (4.8%)

All the patients were reviewed for complications within one year of surgery. Commonest complication was abdominal wound infection which was present in 9 (42.9%) patients.

Out of 9 those patients who had abdominal wound infections, 4 were in UC group and 5 were in FAP group. Anaemia was found in 7 (33.3%) patients after one year of surgery. Out of 7 anaemic patients, 4 were from UC group and 3 were from the FAP group. Two patients (9.5%) developed pelvic abscesses. They were one each from UC and the FAP groups. Two patients (9.5%) developed incisional hernia. They were one each from UC and the FAP groups.

14 (66.7%) patients were sexually active pre-operatively. Out of 14 sexually active patients, 10 (47.6%) were from the UC group and 4 (19%) were from the FAP group. Post-operatively, there was no change in the number of sexually active patients.

One patient in the UC group who had normal sexual function pre-operatively developed complete erectile dysfunction after IPAA.

Table 4. Sexual function

	Ulcerative colitis	Familial adenomatous polyposis
Pre-operatively sexually active	10 (47.6%)	4 (19%)
Post-operatively sexually active	10 (47.6%)	4 (19%)
Erectile dysfunction	1 (4.8%)	0
Dyspareunia	0	1 (4.8%)

Impact of complications on post-operative CGQLS was analysed.

Table 5. Impact of complications on CGQLS

	Pre-op CGQLS Mean	Post-op CGQLS Mean
Abdominal wound infections	0.6383	0.6593
Anaemia	0.6286	0.7366
Pelvic Abscess	0.5650	0.7300
Incisional hernia	0.5500	0.7000

One female patient in the FAP group who had normal sexual function pre-operatively developed superficial dyspareunia after surgery.

Post-op CGQL scores were compared using repeated ANOVA. The differences between the means of post-op CGQL scores of main complications encountered were not statistically significant ($p>0.05$).

Discussion

Ileal pouch-anal anastomosis procedure (IPAA) is the surgery of choice in UC and FAP. In UC, it is carried out when the symptoms are severe and cannot be controlled with medical treatment. But in FAP, it is carried out to prevent the occurrence of malignancy which is inevitable if left untreated. FAP patients are usually detected on screening and they are relatively asymptomatic compared to UC patients.

In 1989, Pemberton et al [3] in a controlled trial compared 298 patients who underwent IPAA with 406 patients with Brooke ileostomy and concluded that after IPAA, patients experienced significant advantages in performing daily activities compared to patients with Brooke ileostomy.

Duminda et al [4] in 2010 in a prospective study concluded

that IPAA increases the CGQL scores in UC group significantly after 1 year. But no significant difference was found in FAP group. Our study was designed to compare CGQL scores against the surgical indication to assess the symptomatic improvement and to describe the occurrence of sexual dysfunction and other complications. When comparing the CGQL scores after one year of surgery against the indication, influence of pre-operative CGQL scores has to be controlled since quality of life of UC group is compromised due to presence of symptoms despite the medical treatment. Compared to a previous study [4], this study showed the same trend of mean CGQL scores pre-operatively and post-operatively after one year. After controlling the influence of pre-operative CGQL scores, no significant difference of post-operative CGQL scores after one year of surgery was found implying that IPAA procedure is acceptable in both UC and FAP.

In assessment of daily stool frequency, significant post-operative reduction was found in UC patients. Despite a major surgical procedure carried out in relatively normal FAP patients, there is no statistically significant rise in daily stool frequency within one year of surgery. Both the above findings favour ileal pouch-anal anastomosis. IPAA has also reduced the number of patients who suffered from gastrointestinal and extra gastrointestinal symptoms after the surgery.

Septic complications were commonly found despite the indication for surgery. Anaemia was another commonly encountered complication which may be preventable. The analysis of impact of complications on CGQL scores showed that despite the complications the IPAA procedure improved the quality of life.

Metcalf et al [5] in 1986 and Damgaard et al [6] in 1995 reported improvement of sexual function following IPAA procedure. In our study, two patients who had normal sexual function pre-operatively developed sexual dysfunctions after surgery. It implies that IPAA can be associated with sexual dysfunction which can be explained by damage to the pelvic nerves during surgery.

Main limitation of the study was the limited number of subjects. This study was done retrospectively and therefore recall bias played a role in obtaining information from the patients.

Conclusion

This study concludes that there is no significant difference of CGQL scores following IPAA procedure in relation to the surgical indication. It also showed that, there is significant reduction of stool frequency per day post-operatively in UC but no difference in FAP. Pouch related complications made no significant difference on post-op CGQL scores. Erectile dysfunction and dyspareunia are possible sexual dysfunctions following IPAA procedure.

All authors disclose no conflict of interest. The study was conducted in accordance with the ethical standards of the relevant institutional or national ethics committee and the Helsinki Declaration of 1975, as revised in 2000.

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SCIENTIFIC ARTICLE

Penile cancer: a case series in two tertiary care teaching hospitals with review of literature

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Keywords: Penile cancer; squamous cell carcinoma; penectomy; inguinal node dissection

Abstract

Introduction

Carcinoma of penis is a very rare disease most commonly affecting elderly men. This rare disease can have terrible and horrifying consequences on the social and emotional life of patients as well as their families. The objective of our case series is to describe the sociodemographic and clinical features, the standard investigations and treatment protocols and follow up of patients who presented to our hospitals.

Methodology

This is a prospective study of fourteen patients admitted in two tertiary care teaching institutions of Kolkata between January 2013 to December 2015 with a histopathological diagnosis of penile cancer.

Results and discussion

Age of patients varied between 45 to 82 years. Duration of disease varied between 3-13 months. Nine patients had palpable inguinal lymphadenopathy and 2 patients had liver metastases. Eight patients underwent partial amputation of penis and 4 patients underwent total amputation.

Conclusion

Penile cancer is a rare disease with devastating consequences. Patients often present late and the primary surgical treatment is often disfiguring. Aggressive surgical treatment of the primary disease and groin remains the cornerstone in the management of high-risk cases.

Introduction

Carcinoma of penis is a rare disease commonly affecting elderly men, with Brazil being the country with highest incidence [1]. It usually refers to squamous cell carcinomas (SCC) of penis, however, it encompasses non-squamous malignant lesions also. It is less frequent in countries with higher socioeconomic status like Europe and United States, accounting for 0.4-0.6% of all malignancies, but comparatively commoner in countries with low and middle socioeconomic status like Africa and South America, representing almost 10% of all malignancies [2]. The peak incidence is seen during sixth decade of life. Of these cases, 19% occur below 40 years and 7% below 30 years. The annual age-adjusted rate of penile cancer is 2.3-8.3 per 100000 men [3].

Poor hygiene, phimosis, dermatitis, regional trauma, smoking and infection with Human Papilloma Virus (HPV) are known etiological factors [4]. Neonatal circumcision is presumed to be a protective factor as the incidence rate of carcinoma of penis is very low in countries where neonatal circumcision is routinely practiced [5]. Ninety five percent of penile cancers arise from squamous epithelium of glans (80%) or foreskin (15%) in the form of ulceroproliferative growth , localized or invading the whole penis.

Figure 1. Ca Penis with left inguinal lymphadenopathy

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Penile cancer can have terrible and horrifying consequences on the social and emotional life of patients as well as their families. Presentation is usually late as it is more prevalent in people from low socioeconomic status who come to the hospital mostly when they are debilitated by the disease. Hence a thorough knowledge about the socio-demographic factors, adoption of potential prevention strategies and aggressive treatment regimes are not only necessary but also essential to mitigate this disease. The objective of our case series is to describe the sociodemographic and clinical features, the standard investigations and treatment protocols and follow up of patients who presented to our hospitals between 2013 – 2015.

Materials and methods

We performed this prospective study with fourteen patients admitted to Department of Surgical Oncology in two tertiary care teaching hospitals in Kolkata between January 2013 to December 2015 with a histopathological diagnosis of penile cancer. History, diagnosis, histopathology reports, extension, stage, margin of resection, treatment and events encountered during follow up period were noted. The international TNM classification system was used for staging. Sociodemographic characteristics, clinical features and histopathological characteristics were subjected to special attention. Patients were followed up every three months during the first follow up year and every six months thereafter, provided there was no complication or recurrence.

Figure 2. Post-op picture after partial penectomy

Results

The demographic, clinical, staging , treatment and follow up data are tabulated in the following two tables (Table 1A & 1B). Age of patients varied between 45 to 82 years. 5 patients had diabetes, 5 patients had hypertension, 3 patients had ischemic heart disease. Duration of disease varied between 3-13 months. All the patients presented with ulcers involving the penis, 9 were p T1 – p T2 and 5 were infiltrating the urethra (p - T3). Nine patients had palpable inguinal lymphadenopathy and 2 patients had liver metastases. Two patients were found to have well-differentiated squamous cell carcinoma, 5 patients were found to have moderately differentiated squamous cell carcinoma, 6 patients were found to have poorly differentiated squamous cell carcinoma and 1 patient had diffuse large B-cell lymphoma. Eight patients underwent partial penectomy and 4 patients underwent total penectomy. Two patients with metastatic disease were treated with palliative amputation and palliative chemotherapy. One patient with lymphoma was treated with primary chemotherapy. The patients were followed up for 8- 48 months. Two patients with liver metastasis progressed during the course of the disease and eventually died.

Review of literature

Penile cancer is a disease of elderly males which may have devastating effect on the lives of patients as well as their families. The age distribution of penile cancer patients in our study was compatible with the literature [6]. Infection by Human Papilloma Virus, smoking, phimosis and poor local hygiene have been described as common etiological factors, while early circumcision has been described to be protective. All the patients in our study were uncircumcised and 6 of them had phimosis. Retention of smegma leads to chronic irritation and inflammation of the glans and prepuce in uncircumcised males which has carcinogenic effects [7]. Circumcision gives protection against penile cancer by preventing development of phimosis, collection of smegma, formation of lichen sclerosus and decreasing the risk of infection by HPV type 16 and 18. More than 40% patients are HPV positive and have positive correlation with number of sexual partners. In our study 5 patients were HPV positive evident by presence of malpigiennes cells infected with HPV i.e. koilocytes.

Glans and prepuce are usually involved early by the disease which gradually engulfs the entire glans, shaft,corpora even up to scrotum [8]. In our study patients had a delay of 4 – 13 months before seeking medical attention. It was mostly due to ignorance, shyness, shame, guilt, fear, lack of pain, lack of education and personal neglect. Penile cancer usually appears as an indurated, painless nodule, warty growth, ulcer or exophytic mass with foul odour and /or bloody or purulent discharge . In our study, besides ulcer, patients also presented with itching, inguinal lump and features of lower urinary tract symptoms (LUTS). More than 95% of the cases are squamous cell carcinoma, however, melanocytic lesions, mesenchymal tumours, lymphomas and metastases have also been reported [9]. In our study poorly differentiated squamous cell carcinoma was most frequent. We performed deep biopsy in all patients to assess the depth of invasion. In case of palpable inguinal lymphadenopathy refractory to conservative treatment, we performed ultrasound guided FNAC which enhanced the micrometa-stasis detection rate.

Table 1A : Demographic, clinical, staging , treatment and follow up data of patients 1-7

Patient	P1	P2	P3	P4	P5	P6	P7
Age	63	55	73	59	52	64	82
Cigarette Smoking	Yes	Yes	Yes	No	No	Yes	Yes
Multiple Sex Partner	Yes	Yes	No	Yes	No	No	No
Foreskin status	Uncircumcised	Uncircumcised	Uncircumcised	Phimosis	Phimosis	Uncircumcised	Phimosis
Location	Glans	Glans, distal shaft	Body	Balanoprepucial groove	Glans, prepuce, distal shaft	Glans, balanoprepucial groove	Effaced Penis
Comorbidity	Nil	DM, HTN	DM	DM,IHD	Nil	HTN	IHD
Duration of disease (months)	5	7	3	8	12	10	6
Clinical feature (Other than ulcer)	Discharge, redness	Bloody discharge , itching	Inguinal lump, penile erythema	Pus discharge, erythema, inguinal lump	LUTS	LUTS	Bloody discharge, Itching, LUTS
T (tumour)	T1	T1	T3	T3	T2	T1	T3
N(node)	N0	N0	N3	N3	N1	N0	N2
M(metastases)	-	-	+	-	-	-	-
Histology	MDSCC	WDSCC	PDSCC	PDSCC	MDSCC	Diffuse Large B-Cell Lymphoma	PDSCC
Presence of Pre –malignant lesion	–	+	+	–	–	–	–
Presence of HPV	-	+	+	-	-	-	+
Preoperative assessment	CT	CT	MRI	MRI	CT	CT	MRI
Treatment of primary tumour	Partial penectomy	Partial penectomy	Total penectomy (palliative)	Total penectomy	Partial penectomy	Primary chemotherapy	Partial penectomy
Treatment of lymph node	Surveillance	Antibiotics, surveillance	Palliative chemotherapy	B/L LND, EBRT.	U/L LND	Primary chemotherapy	B/L LND, EBRT.
Progression during follow-up	-	-	+	-	-	-	-
Death	-	-	+	-	-	-	-
Follow up period (months)	48	36	11	27	32	16	28

DM : diabetes mellitus , HTN : hypertension , IHD : ischaemic heart disease , LUTS : lower urinary tract symptoms , EBRT : external beam radiation therapy , LND : lymph node dissection , WDSCC : well differentiated squamous cell carcinoma , MDSCC : moderately differentiated squamous cell carcinoma , PDSCC : poorly differentiated squamous cell carcinoma , CT : computed tomography , MRI : magnetic resonance imaging .

Table 1B : Demographic, clinical, staging , treatment and follow up data of patients 8-14

Patient	P8	P9	P10	P11	P12	P13	P14
Age	53	45	68	39	55	49	69
Cigarette Smoking	No	No	Yes	Yes	Yes	Yes	Yes
Multiple Sex Partner	No	Yes	Yes	No	No	No	No
Foreskin status	Phimosis	Uncircumcised	Phimosis	Uncircumcised	Phimosis	Uncircumcised	Uncircumcised
Location	Body	Distal shaft	Glans, prepuce	Balanoprepucial groove	Distal shaft, glans	Effaced penis	Body
Comorbidity	DM,HTN	DM,IHD	HTN	Nil	Nil	Nil	HTN
Duration of disease (months)	7	12	4	8	11	13	5
Presenting Symptom (Other than ulcer)	LUTS	Inguinal lump, penile erythema	Bloody discharge, itching, inguinal lump	Pus discharge, erythema, inguinal lump	Discharge, redness.	Bloody discharge, Itching	LUTS
T (tumour)	T2	T3	T2	T2	T1	T3	T2
N(node)	N1	N3	N2	N2	N0	N1	N0
M(metastases)	-	+	-	-	-	-	-
Histology	MDSCC	PDSCC	MDSCC	PDSCC	MDSCC	WDSCC	PDSCC
Presence of Pre –malignant lesion	–	–	+	–	–	–	–
Presence of HPV	+	-	-	+	-	-	+
Preoperative assessment	CT	MRI	MRI	MRI	CT	CT	CT
Treatment of primary tumour	Partial penectomy	Total penectomy (palliative)	Total penectomy	Total penectomy	Partial penectomy	Partial penectomy	Partial penectomy
Treatment of lymph node	U/L LND	Palliative chemotherapy	B/L LND	B/L LND, EBRT.	Surveillance	Antibiotics, surveillance	Antibiotics, surveillance
Progression during follow-up	-	+	-	-	-	-	-
Death	-	+	-	-	-	-	-
Follow up period (months)	42	16	23	8	22	31	46

DM : diabetes mellitus , HTN : hypertension , IHD : ischaemic heart disease , LUTS : lower urinary tract symptoms , EBRT : external beam radiation therapy , LND : lymph node dissection , WDSCC : well differentiated squamous cell carcinoma , MDSCC : moderately differentiated squamous cell carcinoma , PDSCC : poorly differentiated squamous cell carcinoma , CT : computed tomography , MRI : magnetic resonance imaging.

In case of palpable lymphadenopathy with negative FNAC we prescribed 4-6 weeks of antibiotics, followed by repeat FNAC if persistent, followed by excisi-onal lymph node biopsy if still negative but highly suspicious and lastly prophylactic lymphadenectomy. CT or MRI were prescribed when clinical examination was difficult like in obese patients or when gross significant lymphadenopathy was present with high suspicion of pelvic spread. MRI has been proven to have higher sensitivity and specificity in detecting and quantifying nodal burden [10]. Artificial erection with contrast enhanced MRI is often useful where exact T-staging is required for organ-preserving surgery .

Penile cancer most frequently spreads to inguinofemoral lymph nodes. Prepucial lymphatics join the network of cutaneous lymphatics of shaft and drain to superficial inguinal nodes whereas glanular lymphatics in the majority drain directly to the deep inguinal nodes, which in turn drains into deep inguinal nodes. Lung, bone and liver are the commonest sites for metastasis. Metastatic cases may present without locoregional lymphad-enopathy, however, metastatic patients in our study presented with heavy locoregional lymph node burden [11]. Metastatic work-up must be done in a patient with proven positive locoregional lymphadenopathy.

Surgical amputation remains the standard treatment for definitive management of penile cancer along with adjuvant modalities. Glans – sparing procedures like limited excision with or without circumcision, Mohs micrographic surgery, laser therapy and radiotherapy may be offered in early stage (Tis,Ta,T1) tumours with favourable histology with the aim of preservation of penile length and sensation.

In our study we preferred conventional partial or total amputation in patients presenting with high stage, significant lymphadenopathy and non-favourable histologies . As per literature, in case of partial amputation we spared a stump of at least 2-3 cm [12]. We performed palliative amputation even in metastatic setting to offer a better quality of life to the patients and their families. Primary chemotherapy was given in a solitary patient of diffuse large B-cell lymphoma without any surgical intervention.

Surgical intervention of groin is indicated in patients with significant inguinal lymphadenopathy, either non-responding to medical management or proven as metastatic by FNAC. Decision regarding extent of lymphadenectomy is critical because it carries significant morbidity as high as 50% [13]. Complications like surgical site infection (1.2-1.4%), flap necrosis (0.6-4.7%), lymphoedema (5-13.9%), lymphocele (2.1-4%), phlebitis and rarely pulmonary embolism[14] have been reported. However, Catalona's technique of modified superficialinguinal lymphadenectomy may reduce complication rates with similar long term results [15], but radical procedure must be followed if invasion of lymph node is confirmed histologically.

None of our patients were offered primary chemotherapy except those with metastases who required palliative chemotherapy (bleomycin, cisplatin, methotrexate) and a patient with lymphoma who received primary chemotherapy. Adjuvant chemotherapy may be offered after surgical resection in high risk patients. Cisplatin has shown promising result in presence of large, immobile, palpable inguinal nodes, even as neoadjuvant. Palliative chemotherapy has been used in unresectable primary tumours, fixed, bulky or relapsed inguinal nodes and in presence of distant metastasis but without much promising result [16]. Adjuvant radiotherapy was prescribed depending on positive lymph nodes, perineural or lymphovascular invasion, margin status and extra-capsular extension. Usually clinically palpable lymphadenopathy is found in 28-64% of patients, 47-85% of which are due to metastasis and rest due to infection and inflammation. 12-20% of patients without palpable lymph nodes harbour occult metastasis [17]. Early inguinal lymphadenectomy is prognostically better than surveillance and delayed lymphadenectomy [18].

In advanced cases (T1,G3 or T2-4) aggressive management of groin is highly solicited. There is no role of curative radiotherapy in metastatic groin nodes. Low and intermediate risk cases (Tis, Ta , T1 G1-2) can be managed by cautious surveillance but high risk cases (T2-4) should be offered bilateral superficial inguinal lymphadenectomy with frozen section or complete lymphadenectomy (modified or radical). Dynamic sentinel node biopsy has high sensitivity in detecting clinically occult groin nodes with low morbidity compared to complete lymphadenectomy [19].

Regular follow-up of the patients were done for at least 2 years as 74.3% of all recurrences, 66.4% of local recurrences, 86.1% of regional recurrences and 100% of distant recurrences are known to occur within first two post-operative years [20]. Our patients were followed up every 3 months during the first post-op year and every 6 months during the 2nd post-op year in absence of progression or oncological recurrence.

Conclusion

Patients with penile cancer often present late and the primary surgical treatment is often disfiguring. HPV is an important risk factor. Early circumcision, though reducing incidence, does not offer total protection. Lymph node involvement appears to be the main prognostic factor, therefore, accurate staging and appropriate decision-making regarding groin is of utmost importance. Aggressive surgical treatment of the primary disease and groin remains the cornerstone in the management of high-risk cases. However, a larger series is required to establish standard integrated multimodality treatment protocol for this deleterious disease.

All authors disclose no conflict of interest. The study was conducted in accordance with the ethical standards of the relevant institutional or national ethics committee and the Helsinki Declaration of 1975, as revised in 2000.

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SCIENTIFIC ARTICLE

A clinicopathological study of morphological pattern and management of parotid tumours: a multicentric experience

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Keywords: Salivary gland tumour; pleomorphic adenoma; mucoepidermoid carcinoma.

Abstract

Introduction

Parotid tumours are heterogeneous neoplasms with complex morphology and dubious clinical characters. The aim of our study was to assess the demographics, frequency, morphology, management & long term follow up results of the patients undergoing parotidectomy.

Methodology

This prospective study was conducted on all parotidectomies performed at the Dept. of Surgery and Surgical Oncology of three premiere teaching institutes of Kolkata between January 2011 to December 2015.

Result and discussion

The mean age of presentation in our study was comparable with other series [9,10]. Pleomorphic adenoma was most common with 51 (41.5%) patients and Warthin's tumour was 2nd most common with 19 (15.4%) patients. Permanent facial nerve palsy was seen in 0.04% of our patients. Pain (41.3%) and swelling (100%) were the most frequent presenting feature of malignancy. 15 (34%) patients with malignant tumour required additional reconstruction by pectoralis major myocutaneous flap.

Conclusion

Our study came out with many similarities in clinical course of parotid tumours in other parts of the world as well as a few individual findings. Surgery with optimum preoperative planning and counselling remains the mainstay of treatment.

Introduction

Salivary gland tumours are heterogeneous neoplasms with complex morphology and dubious clinical characters. They represent about 3% of all tumours and 5-6% of all head and neck tumours. 80% of these tumours are located in the parotid gland, of which, 80% are benign, limited in lower part of the gland and 80% of them are pleomorphic adenomas. Ninety percent of them arise from the superficial lobe[1]. These tumours represent a challenging clinical entity to the clinicians due to their wide spectrum of presentation, inconsistent clinical features, management protocols and unpredictable prognosis.

Parotid tumours are more frequent in females. Ionising radiation, exposure to sunlight, chemotherapy, smoking, Vitamin A deficiency, geographic location and ethnicity have been linked with their incidence. They appear as slow growing tumours with a visible swelling in the parotid region being the only feature in majority of the cases. Rapid enlargement, tenderness or neuropathy often signifies malignancy, tuberculosis or sarcoidosis [2]. Common malignant tumours are adenoid cystic carcinoma, mucoepidermoid carcinoma and adeno-carcinomas.

Fine Needle Aspiration Cytology (FNAC) is often the first pathological investigation with sensitivity and specificity of approximately 95% and 75% [3]. Although CT scan helps in delineating the extent of the lump, involvement of deep lobe, parapharyngeal extension and relation to facial nerve, MRI is considered as investigation of choice [4]. Relationship of the tumour with facial nerve warrants careful and cautious dissection during parotid surgery because unintentional injury or sacrifice of facial nerve leads to life-long disfigurement with discouraging result even after reanimation surgery .

The aim of our study was to assess the demographics, frequency, morphology, management and long term follow up results of the patients undergoing parotidectomy at three tertiary care centres of Kolkata between January 2011 to December 2015.

Materials and methods

A prospective study was performed on all parotidectomies performed at the Department of Surgical Oncology, B.R. Singh Hospital & Research Centre, Department of General

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Surgery, Medical College & Hospital, Kolkata and IPGMER & SSKM Hospital between January 2011 to December 2015. A total of 167 patients who underwent parotidectomy were identified. Data collected included patient particulars, detailed history, physical examination, USG/ CT / MRI scans, cytopathology and histopathological reports, ancillary investigations, type of surgery, postoperative events & follow up.

Inclusion criteria - all patients presenting with parotid tumours regardless of age and sex.

Exclusion criteria - inflammatory parotid swellings , parotid abscesses, post-traumatic parotid swellings, history of tuberculosis, sarcoidosis or prolonged alcoholism or steroid intake .

Results

Between January 2011 and December 2015, 167 patients underwent parotidectomy. Amongst them, 82 were male (49.1%) and 85 were female (50.9%). The mean age of presentation was 36 years for benign tumours with range between 22 – 76 years and 48 years for malignant tumours with range between 25 – 71 years. All the patients had FNAC performed prior to surgery. All the patients had CT / MRI scan performed before operation to assess the extent of the lesion.

Benign tumours were 123 (73.65%) and malignant tumours were 44 (26.35%) as per the final histopathology report . Among benign tumours pleomorphic adenoma was the most common (41.5%), of which 30 cases were found in females and 21 cases in males. Other benign tumours found in this series were recurrent pleomorphic adenoma (8.1%), monomorphic adenoma (8.9%), Warthin's tumour (15.4%), lipoma (2.4%), Schwannoma (7.3%), neurofibroma (5.7%), myoepithelioma (5.7%) and lymphoepithelial cysts (4.9%). All benign tumours presented with swelling in parotid region for months to years.

Most common malignant tumour in this series was mucoepidermoid carcinoma, 12 cases, 27.3% of malignant parotid tumours and 7.2 % of all parotid tumours. Other malignant tumours were adenoid cystic carcinoma (11.4%), acinic cell carcinoma (11.4%), carcinoma-ex-pleomorphic adenoma (11.4%), undifferentiated carcinoma (4.5%), salivary duct carcinoma (6.8%), poorly differentiated carcinoma (4.5%), basal cell adenocarcinoma (4.5%), myoepithelial carcinoma (2.3%), polymorphous low grade adenocarcinoma (4.5%), squamous cell carcinoma (2.3%), adenocarcinoma not otherwise specified (4.5%), sarcoma (2.3%) and lymphoma (2.3%). Pain (41.3%) and swelling (100%) were the most common symptoms in malignant parotid masses, followed by skin fixity (16.2%), underlying tissue fixity (9%), cervical lymphadenopathy (17.4%) and facial nerve palsy (3.6%).

Superficial lobe was the most frequent site involved by both benign and malignant tumours. Ninety eight (79.7%) benign tumours originated from the superficial lobe and 25(20.3%) tumours involved deep lobe, whereas all malignant tumours involved superficial lobe only.

Ninety eight (58.7%) out of 167 patients underwent superficial parotidectomy and 69 (41.3%) patients underwent total parotidectomy. Among 69 patients undergone total parotidectomy 25 were benign and 44 were malignant tumours. 25 patients with benign parotid tumours underwent total parotidectomy with facial nerve sparing as the tumour involved the deep lobe in addition to superficial lobe. 38 patients with malignant tumours had total parotidectomy with sparing of facial nerve macroscopically whereas 6 patients with malignant parotid tumours had total parotidectomy with facial nerve resection. Twenty nine patients underwent modified radical neck dissection with total parotidectomy because of palpable or radiologically significant neck nodes. Reconstruction by PMMC (Pectoralis Major Myocutaneous Flap) was required in 15 patients.

Eight patients developed post-operative hematoma which settled with aspiration or evacuation. Eleven patients developed wound infection following operation which resolved with intravenous broad-spectrum antibiotics and regular dressing. Hundred and thirty four (80.24%) patients had transient facial nerve palsy (House Brackman Grade 2 or 3) that resolved with steroids or spontaneously with time within 2-8 weeks. 6 (0.04%) patients with severe facial nerve had complete facial nerve palsy (House Brackman Grade 6) [5]. The mean follow up period after surgery was 9 months with range of 1-18 months.

In the follow up period we found that all the benign cases remained healthy without any mortality, among the malignant cases 22 patients (13.2%) with high grade malignancies died because of local or distant recurrence, 12 patients (7.2%) with intermediate grade malignancies are living with the disease, in the form of either local or distant recurrence, rest 10 patients (6%) are living without any recurrence or residual disease .

Table 1. Demographic, clinical, operative and post-operative data

No. of patients	**167**
Male/ Female	82/ 85
Left/ Right	96/71
Age in years	42 (range 22-76)
FNAC (Benign/ Malignant)	115/ 40 (12 – inconclusive)
Histology (Benign/ Malignant)	123/ 44
Parotidectomy (Superficial/ Total)	98/ 69
Mean follow up after surgery (months)	9 (range 1-18)

Table 2. Distribution of patients by age

Age in years	Benign tumours	Malignant tumours
21-30	2	2
31-40	43	8
41-50	40	11
51-60	22	15
61-70	13	7
71 and above	3	1
Total	123	44

Table 3. Distribution of patients by clinical features

Clinical feature	Number	Percentage (%)
Swelling	167	100
Pain	69	41.3
Skin involvement	27	16.2
Fixity with underlying muscle and/or bone	15	9
Enlargement of deep lobe	25	15
Facial nerve palsy	6	3.6
Palpable cervical lymphadenopathy	29	17.4

Table 4. Distribution of patients as per final histopathology report

MALIGNANT	44	26.3%
Mucoepidermoid Carcinoma	12	27.3%
Acinic cell carcinoma	5	11.4%
Adenoid cystic carcinoma	5	11.4%
Adenocarcinoma NOS	2	4.5%
Squamous cell carcinoma	1	2.3%
Lymphoma	1	2.3%
Sarcoma	1	2.3%
Carcinoma ex-pleomorphic adenoma	5	11.4%
Undifferentiated carcinoma	2	4.5%
Poorly differentiated carcinoma	2	4.5%
Salivary duct carcinoma	3	6.8%
Basal cell adenocarcinoma	2	4.5%
Myoepithelial carcinoma	1	2.3%
Polymorphous low grade adenocarcinoma	2	4.5%
BENIGN	**123**	**73.6%**
Pleomorphic adenoma	51	41.5%
Warthin'stumour	19	15.4%
Recurrent pleomorphic adenoma	10	8.1%
Monomorphic adenoma	11	8.9%
Lipoma	3	2.4%
Schwannoma	9	7.3%
Neurofibroma	7	5.7%
Myoepithelioma	7	5.7%
Lymphoepithelial cyst	6	4.9%

Table 5. Post-Parotidectomy Complications

COMPLICATION	Number	%
Haematoma	8	4.8
Wound infection	11	6.59
Facial nerve palsy (Transient)	114	68.26
Facial nerve palsy (Complete)	6	0.04
Recurrence	7	4.2
Flap Necrosis (PMMC)	2	1.2
Frey' syndrome	4	2.4
Salivation from wound	12	7.2
Ear numbness	43	25.75
General anaesthesia complications	5	3

Discussion

Salivary gland tumours are the most complex and morphologically diverse group of human tumours with different clinical features, varied morphology, dubious nature and unpredictable prognosis [6]. These tumours have infectious, granulomatous , auto-immune, obstructive, developmental, idiopathic and neoplastic etiology [7]. Most often they present as non-tender gradually progressive masses in respective regions. Most of them occur in the parotid gland and most of them are benign. Commonest form of benign salivary gland tumours is pleomorphic adenoma , both in major and minor salivary glands.

Incidence of parotid tumour is approximately 2.4/100,000/ year [8]. The mean age of presentation in our study was comparable with other series [9,10]. In contrast to literature, left sided tumours were more frequent and female preponderance was more in our study [11].

Benign tumours accounted for 73.6% of parotid tumour in this study. Pleomorphic adenoma was most common with 51 (41.5%) patients and Warthin's tumour was 2nd most common with 19 (15.4%) patients. Incidence of malignant tumours (26.3%) was compatible with other published data [12,13]. Mucoepidermoid carcinoma was the commonest malignant tumour of the parotid gland in the present study, 12 patients (27.3%) similar to literature.

All the patients had CT/MRI scan performed preoperatively to assess the extent of tumour and treatment planning. MRI was very useful particularly in patients with deep lobe involvement, suspected malignant tumours with local infiltration, recurrent cases and tumours extending to inaccessible areas such as retromandibular fossa or parapharyngeal space [14].

The incidence of transient facial nerve palsy was 68.26% in our study, higher than studies reported by Laccorreye [15] & Mehle [16]. Permanent facial nerve palsy was seen in 0.04% of our patients. Of the 6 cases who had complete nerve palsy, 3 had mucoepidermoid carcinoma, 2 had adenoid cystic carcinoma and 1 had poorly differentiated carcinoma with nerve entrapment. This result was similar to other studies (0-10%) [17].

Thorough anatomical knowledge and nerve stimulator are extremely necessary for facial nerve preservation. Patients with malignancy were preferentially treated with total parotidectomy with or without facial nerve sparing as compared to benign disease with a low threshold for nerve sacrifice.

Recurrence rate of pleomorphic adenoma in the present study was 8.1%, and rate of malignant transformation was 11.4% higher than many larger series (<2%) [18]. Surgery for these two entities was technically very challenging with increased morbidity and worse prognosis.

Pain (41.3%) and swelling (100%) were the most frequent presenting feature of malignancy in our study similar to the literature, however, skin or underlying tissue fixity and cervical lymphadenopathy have also been reported in other series as common features [19].

Surgery was the mainstay of treatment in our series. However,14 patients (31.8%) received neoadjuvant chemotherapy, 4 patients (9%) received adjuvant chemotherapy and 38 patients (86.36%) received adjuvant radiotherapy. 15 (34%) patients with malignant tumour required additional reconstruction by PMMC flap.

Conclusion

The current study is a prospective study of parotid tumours in three tertiary care hospitals of Kolkata over a span of 5 years. The approach was to study morphological and histopathological distribution of parotid tumours, classification, difficulties encountered during management and to compare with the observations in similar studies with special emphasis on incidence, age, sex and complication rates.

Our study found many similarities in clinical course of parotid tumours when compared to other parts of the world, as well as a few unique findings. Female preponderance was found with more tendency of left sided tumours. Average age of incidence was higher for malignant neoplasms than their benign counterparts . Pleomorphic adenoma was the most common benign parotid gland tumour and mucoepidermoid carcinoma was the most frequent malignant neoplasm . Surgery with optimum preoperative planning and counselling remains the mainstay of treatment . Prior and in-depth knowledge of regional anatomy with meticulous and careful planning and use of advance technology is essential to reduce the incidence of complications.

All authors disclose no conflict of interest. The study was conducted in accordance with the ethical standards of the relevant institutional or national ethics committee and the Helsinki Declaration of 1975, as revised in 2000.

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REVIEW ARTICLE

Update on antibacterial agents: current challenges and recent initiatives

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Abstract

Antibacterial agents (ABAs) contribute significantly to reduce morbidity and mortality of bacterial infections as well as play a crucial role in the success of major advances in medicine such as organ transplants, advanced surgeries, cancer chemotherapy and cardiac surgery. However, their success as well as their very existence itself are under threat due to two major problems, one is antibacterial resistance (ABR) and the other is discovery void.

A 2014 report by the World Health Organization (WHO) warns that bacteria that cause common health-care associated and community-acquired infections exhibit high resistance rate in all WHO regions. This threat has been endorsed by many organizations including Centres for Disease Control and Prevention (CDC), Infectious Diseases Society of America, and other UN bodies. Though bacteria can develop resistance spontaneously through mutation, the escalating public health threat of ABR is mainly driven by both appropriate and inappropriate use of ABAs in humans, animals, food production, agriculture, and aquaculture. Several initiatives at different levels have been launched to combat ABR.

Development of new ABAs which feature new target or mode of action by pharmaceutical industries has the potential to address the problem of ABR. However, hardly any new ABAs featuring new target or mode of action came to market in the last two decades due to economic and regulatory obstacles. Collaboration between industry, government bodies and academic institutions in the exploration of new ABAs, offering incentives, fast tracking market authorization are some of the initiatives recommended by the WHO to address this issue of dry antibiotic pipeline. Rational use of ABAs, implementation of antibiotic stewardship programmes, and adherence to strategies which minimise spread of resistant bacteria such as hand-washing and infection control measures are few key activities that can be incorporated in clinical practice.

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Introduction

Antibacterial agents (ABA) have saved millions of lives. Not only do they contribute significantly to reduce morbidity and mortality of individual classic infectious diseases, but also serve a crucial role in the success of modern medicine such as advanced surgical procedures, organ transplants, cancer chemotherapy, neonatal care and intensive-care. However, the achievement of ABAs is currently under threat as antibacterial resistance (ABR) is escalating at an exponential rate. This review presents an overview of current trends of ABR and few key global and national initiatives towards combating ABR.

ACCESS, WATCH and RESERVE antibacterial agents

The World Health Organization (WHO) recently revised the entire antibacterial agents section in the model essential medicine list (EML) [1]. This was the biggest revision in the 40- year history of WHO Model EML. The WHO Expert panel on selection and use of essential medicines has grouped the ABAs into three categories namely ACCESS, WATCH and RESERVE which is accompanied by recommendations on indications for each category. The list encompasses ABAs for 21 most common general infections which includes urinary tract infections, skin and soft tissue infections, surgical site infections, hospital acquired pneumonia, complicated intra-abdominal infections and bone and joint infections. It is postulated that this categorization will ensure access to ABAs when needed, rational prescription of right ABAs for right infections, improve treatment outcomes, reduce the development of drug-resistant bacteria, and conserve the effectiveness of "last-resort" ABAs that are needed when all others fail. Comprehending the rationale for this categorization is important to use this categorization in clinical practice and policy making.

Antibacterial agents which are either first or second choice in at least one of the above 21 syndromes are classified as ACCESS ABAs (Table 1) [1].

"These essential ABAs are those that satisfy the priority health care needs of the population and intended to be available within the context of functioning health systems at all times in adequate amounts, in the appropriate dosage

Table 1. Antibacterial agents listed in ACCESS group

Beta-lactam medicines		Other antibacterial	
amoxicillin	cefotaxime*	amikacin	gentamicin
amoxicillin + clavulanic acid	ceftriaxone*	azithromycin*	metronidazole
ampicillin	cloxacillin	chloramphenicol	nitrofurantoin
benzathine benzylpenicillin	Phenoxymethyl penicillin	ciprofloxacin*	Spectinomycin (EML only)
benzylpenicillin	piperacillin + tazobactam*	clarithromycin*	sulfamethoxazole + trimethoprim
cefalexin	procaine benzyl penicillin	clindamycin	vancomycin (oral)*
cefazolin	*meropenem**	doxycycline	*vancomycin (parenteral)*

Italics = complementary list in the essential medicine list

*Watch group antibiotics included in the essential medicine list only for specific, limited indications

Table 2. Antibacterial agents listed in WATCH group

Quinolones and fluoroquinolones: e.g. ciprofloxacin, levofloxacin, moxifloxacin, norfloxacin
3rd-generation cephalosporins (with or without beta-lactamase inhibitor): e.g. cefixime, ceftriaxone, cefotaxime, ceftazidime
Macrolides: e.g. azithromycin, clarithromycin, erythromycin
Glycopeptides: e.g. teicoplanin, vancomycin
Anti-pseudomonal penicillins with beta-lactamase inhibitor: e.g. piperacillin + tazobactam
Carbapenems: e.g. meropenem, imipenem + cilastatin
Penems: e.g. faropenem

Table 3. Antibacterial agents listed in RESERVE (last-resort) group

Aztreonam	Fosfomycin (IV)
4th generation cephalosporins e.g. cefepime	Oxazolidinones e.g. linezolid
5th generation cephalosporins e.g. ceftaroline	Tigecycline
Polymyxins e.g. polymyxin B, colistin	Daptomycin

forms, with assured quality, and at a price the individual and the community can afford. They are selected on the basis of disease prevalence, evidence on efficacy, safety and comparative cost-effectiveness [2]".

The main function of the WHO EML expert committee is to update the WHO model EML which is done every 2 years. In previous years, the committee stopped with selection of essential ABAs (ACCESS group). The 2017 committee extended its role and categorized the remaining ABAs into two groups mainly to assist ABA stewardship programmes. The "WATCH" group includes ABA classes that are recommended as first or second choice treatments for a limited number of indications, but are flagged as having high resistance potential (Table 2). The RESERVE group identifies ABAs that should be considered as last-resort when other alternatives would be inadequate or have already failed (e.g., serious life-threatening infections due to multi-drug resistant bacteria). They are expected to be personalized to highly specific patients and settings (Table 3). Understandably, there are some overlaps: For example, some ABAs in the ACCESS group are listed under WATCH group as well since there are concerns about resistance. Their use should be monitored.

The message delivered is: Ensure "universal access" to first group, "watch" the use of second group and "reserve" the third group as much as possible. Considerable amount of background work has been done by a group of global experts on adult and paediatric infectious diseases as well as by the members of the WHO expert committee representing both resource limited and rich countries in formulating this categorization. It is highly recommended that the healthcare professionals, administrators and policy makers give serious attention to this recommendation if interested in combating antibacterial resistance (ABR). This aim of this classification is to guide rational choice of ABAs and not function as guidelines. The expert committee stressed that the treatment decisions will depend on local/national uniqueness including availability of ABAs and local resistance patterns; hence clinical judgment would be the decisive factor when it comes to treatment of an individual patient.

National Guidelines for empirical and prophylactic use of antimicrobials

In 2016, the Sri Lanka College of Microbiologists in collaboration with the other professional colleges in healthcare and the Ministry of Healthcare and Nutrition published the National Guidelines for the empirical and prophylactic use of antimicrobials [3]. Twenty Professional Colleges and Associations including the College of Surgeons have contributed in developing the guidelines. It gives the

national recommendations for 22 infections which require ABAs. Examples include bacterial endocarditis, bone and joint infections, intra-abdominal infections, surgical-prophylaxis, urinary tract infections in adults, childhood urinary tract infections and trauma prophylaxis. Each infection is further categorized and recommendations for primary and alternative therapy are listed. Details of agent, dose and route of administration are indicated. In addition, relevant comments for example, investigations to be done, decision about duration of therapy, important precautions, etc can be found.

Any guidelines on use of antimicrobials cannot give definitive recommendation because ABAs had to act against living organisms. Virulence and resistance of these living organisms dictate the final decision which differs from patient to patient, setting to setting and time to time. The Sri Lankan guidelines clearly indicate that the ABA should be tailored whenever a microbiological diagnosis and antibiotic susceptibility results are available. The guidelines will be a very useful guide for a clinician, especially when rapid microbiological diagnostic facilities are not available. However, it will not substitute clinical acumen and hospital level data on antibacterial sensitivity. In addition, treating an infection successfully goes beyond the boundaries of selecting the correct ABA. Pharmacokinetics and dynamics play key role in successful treatment of an infection [4]. Hence, rational use of ABAs and adherence to other strategies which combat ABR such as hand-washing, infection control, etc. are equally important. The guidelines is available for free downloading in the College of Microbiologists website (slmicrobiology.net/download/National-Antibiotic-Guidelines-2016-Web.pdf)

Surgical prophylaxis and surgical-site infection (SSI)

Guidelines for surgical prophylaxis are available in his National Guidelines. Surgical procedures have been classified clean, potentially contaminate (clean contaminated), contaminated and dirty (infected) as per the National Institute for Health and Care Excellence-UK (NICE-UK, 2008) classification [5]. Antibacterial prophylaxis is indicated in some clean (e.g.; surgery involving introduction of prosthetic material, surgery where consequences of infection would be catastrophic like open heart surgery and surgery with impaired host defence) and all clean-contaminated surgeries. For contaminated surgeries either ABA prophylaxis or therapy is recommended depending on patient's clinical condition and for dirty surgeries ABA therapy is indicated. It also outlines patient care recommendations, and recommended agent/s. dose, duration and timing of ABA prophylaxis. Recently both WHO and Centres for Disease Control and Prevention (CDC) have published extensive stand-alone guidelines on surgical – site infections [6,7].

Non human-use of antibacterial agents

Use of ABAs in veterinary medicine, food-animal industry, livestock production (mainly poultry, cattle, turkeys and pigs), agriculture and aquaculture contributes significantly to development and spread of ABR [8-10]. Infections caused by these resistant bacteria are transmitted to humans via food-chain, contaminated hands and environment.

In USA, it is estimated that about 1 in 5 resistant infections are caused by germs from food and animals [11]. Polypeptides, macrolides, quinolones and penicillins are approved for non-therapeutic use (growth promotion) in animal agriculture. Fish-farming industry uses ABAs to prevent disease, promote growth, increase yield and treat infections. In animal husbandry, ABAs are often used in sub-therapeutic doses for a longer period of time. When few animals are affected by an infection, the entire group is treated with ABA irrespective of whether they are sick or healthy [8-10]. Already, European Union has imposed a ban on feeding antibiotics to livestock for growth promotion [9].

In this context, the recently published 5th revision of critically important antimicrobials (CIA) for human medicine by the World Health Organization Advisory Group on Integrated Surveillance of Antimicrobial Resistance [12] is a crucial initiative. It is a collaborative effort of Food and Agriculture Organization of the United Nations (FAO), the World Organization for Animal Health (OIE), and World Health Organization (WHO). Key object of this list is to rank medically important antimicrobials for risk management of antimicrobial resistance due to non-human use.

The list classifies ABAs into three namely [1] critically important, [2] highly important and [3] important for human medicine. Antimicrobials listed under critically important group are the “sole or one of limited available therapies, to treat serious bacterial infections in people” and “used to treat infections in people caused by either: [1] bacteria that may be transmitted to humans from non-human sources, or [2] bacteria that may acquire resistance genes from non-human sources”. Example includes cephalosporin (3rd, 4th and 5th generation), glycopeptides, macrolides, ketolides, polymyxins and quinolones.

Recently, the National Strategic Plan for combating antimicrobial resistance (2017-2022) was launched in Sri Lanka as a collaborative programme of Ministries of Health, Fisheries and Aquatic Resources Management, Agriculture and Rural Economy with the support and concurrence of the World Health Organization [13]. There are five strategies [1] Improve awareness and understanding of antimicrobial resistance through effective communication [2] strengthen the knowledge and evidence base surveillance and research [3] reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures [4]

optimize the use of antimicrobial medicines in human and animal health [5] prepare the economic case for sustainable investment and increase investment in new medicines, diagnostic tools, vaccines and other interventions. Each strategy has specific objectives and mile-stones to achieve.

Integrated surveillance of antimicrobial resistance and use

Surveillance of ABR and ABA use is an essential component to contain ABR [14]. The European Surveillance of Antimicrobial Consumption network (ESAC-Net) has demonstrated that monitoring antimicrobial use patterns and costs is an important resource for advocacy at local or national level, especially when surveillance of use is enhanced by surveillance of resistance [15]. Three surveillance programmes in Sri Lanka need special mention.

Surveillance of antimicrobial resistance

In 2011, the Sri Lanka College of Microbiologists, in collaboration with the Ministry of Healthcare initiated the National Laboratory Based Surveillance of Antimicrobial Resistance. The goal was to survey the pooled susceptibility of significant isolates (colony count ≥105 CFU/ml) cultured from urine of non-catheterized patients. In 2014, data from seven centres showed that the majority (80%) of isolates were coliforms with a very high resistance rate for ampicillin (90.1%).

Those isolated from adults attending outpatient clinics were most susceptible to meropenem (100%) followed by imipenam (97.4%), gentamicin (86.4%), nitrofurantoin (65.1%), cefota-xime (63.4%), cephalexin (55.2%), cephradine (55.2%), amoxicillin/clavulanic acid (54%) and norfloxacin (48.3%). Those isolated from adult hospitalized patients were most susceptible to meropenem (87.9%) followed by gentamicin (62.6%), cefotaxime (39.5%) and ciprofloxacin (31.9%). Resistance rate was comparatively less with coliforms isolated from paediatric out-patients [16].

Secondly, in 2013, the Sri Lanka College of Microbiologists reported the results of Antimicrobial Resistance Surveillance Project (ARSP) of Phase 1.

This surveillance programme exa-mined the Gram negative bacteria and their susceptibility to ABAs in patients who were clinically managed as bacterae-mia in seven hospitals during 2009-2010 period: Of the 733 Gram negative isolates studied, ESBL producing Escherichia coli and Klebsiella pneumonia accounted for 22.5%.

They were most susceptible to meropenem and imipenam (100%) followed by amikacin (80-85%) and netilmicin (65-67%). Susceptibility to gentamicin and ciprofloxacin was poor. In addition, a high level of ciprofloxacin resistance was seen among Salmonella paratyphi (90%) and typhi (50%) isolates [17].

Integrated surveillance of antimicrobial resistance and use in Colombo district

Having computerized data, extensive inter-connected surveillance networks, adequate laboratory capacity and rapid diagnostic facilities played a key role in the success of ESAC-Net and similar programmes established in resource-rich countries. In most of the resource-limited countries (RLCs), such resources are scarcely available. Hence, in order to assist RLCs to carry out efficient surveillance programmes, the WHO published a model for Community-Based Surveillance of Antimicrobial Use and Resistance in Resource-Constrained Settings based on five pilot projects conducted in India [3] and South Africa [2, 14].

For surveillance of antibacterial resistance, the model recommends monitoring the resistance pattern of Escherichia coli (E. coli) isolated from urine samples of patients with urinary tract infections presented to public and private outpatient departments. For ABA use data, the model recommends collecting data from multiple facilities, both from the public and private sectors, from which people living in the geographical area might obtain ABA for ambulatory use. This model was piloted in the Colombo district.

In the public sector, of the 2183 urine samples, pathogenic E. coli was isolated in 9.3% (204), and 8% (n=16) of them were Extended Spectrum Beta Lactamase (ESBL) producers. E. coli was most resistant to ampicillin (85%), followed by nalidixic acid (58.5%), trimethoprim/sulphamethoxazole (47.1%), ciprofloxacin (46.2%), norfloxacin (43.7%) amoxicillin /clavulanic acid (36.3%), gentamicin (23%) and nitrofurantoin (9%). Multi-drug resistance was seen in 44% (18). In the private sector, of the 969 pathogenic E. coli, 28% were ESBL producers. E. coli was most resistant to ampicillin (80%) followed by nalidixic acid (67.8%), ciprofloxacin (59.5%),norfloxacin(59%),trimethoprim / sulphamethoxazole (52.5%), amoxicillin /clavulanic acid (44%), gentamicin (33%) and nitrofurantoin (15%) Multi-drug resistance was seen in 53% (Senadeera et al, unpublished data).

Empirical use of ABAs with high resistance rates is known to be associated with an increased risk of treatment failure and selection of resistant strains. Surveillance of ABA use (Senadeera, et al, unpublished data) documented that of a total of 22321 prescriptions containing at least on ABA, amoxicillin /clavulanic acid accounted for 17.5% followed by amoxicillin (15%), cefuroxime (11%), azithromycin (8%), doxycycline (7.8%), clarithromycin (7.1%), ciprofloxacin (6.5%) and levofloxacin (5.1%). From this data, one may predict that resistance to amoxicillin /clavulanic acid would also escalate similar to what has happened amoxicillin.

Drivers for these initiatives

These accelerated initiatives are mainly due to two reasons: Escalating problem of ABR and the broken antibiotic

pipeline. Resistance to ABA is defined clinically as "a state in which a patient, when infected with a specific pathogen, is treated with an adequate antimicrobial dosage and administration schedule, but clinical criteria of cure (at a clinical and/or a microbiological level) are not reached" and microbiologically as "a state in which an isolate has a resistance mechanism rendering it less susceptible than to other members of the same species lacking any resistance mechanism" [19]. Alarming findings documented in a WHO global surveillance report published in 2014 inclde [20]:

1. Klebsiella pneumonia: Resistance to third-generation cephalosporin was > 30% in many countries and > 60% in some countries. Resistance to carbapenems exceeding 50% has reported
2. Escherichia coli: Resistance to fluoroquinolones and third generation cephalosporin > 50% in 5 out of 6 WHO regions
3. MRSA resistance rates > 20 % in all WHO regions and in some regions it is > 80%

The report documented very high rates of ABR in bacteria causing common health-care associated and community-acquired infections in all WHO regions and identified important gaps in existing surveillance programmes such as lack of data from countries with high disease rates and lack of standards for methodology.

Many pharmaceutical companies have abandoned the field of development of new ABA as it needs long time and huge investment. Only handful of the big pharmaceutical industries still continue to work on ABA development programmes, with others have closed the antibiotic research facility and manufacturing drugs that have proven sustainability in the market [9]. The three main factors responsible for pharmaceutical industries' lack of interest in antibiotics include:

1. Scientific: Most of the known drug targets have been already exploited.
2. Commercial: ABAs have limited prospects for profit as they are generally prescribed for short duration and most of the times cure the target disease. In addition, when the bacteria develop resistance, the demand for that ABA dramatically declines.
3. Regulatory bottlenecks: The regulatory requirements have become very demanding.

There is an urgent need to fix the broken antibiotic pipeline: In 2010, the Infectious Diseases Society of America launched the "10 X 20" initiative with the aim of producing 10 new antibiotics by 2020. In the first 6 years (2010-2016), though 6 new ABAs have received FDA approval, only one was a novel compound [21]. The WHO has published the global priority list of antibiotic-resistant bacteria to guide research, discovery and development of new ABAs [22]. Pathogens listed under critical priority are carbapenem-resistant Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacteriaceae and third-generation cephalosporin-resistant Enterobacteriaceae. Pathogens like clarithromycin-resistant Helicobacter pylori, fluoroquinolone-resistant Salmonella spp., third-generation cephalosporin-resistant Neisseria gonorrhoea, and fluoroquinolone-resistant Neisseria gonorrhoea are listed under second priority level. Penicillin non-susceptible Streptococcus pneumonia is in the 3rd level.

Antibacterial agents' stewardship programmes

Antibacterial agents' stewardship programme (ASP) is a hospital-level programme committed to improve use of ABAs [23]. The CDC recommends that all acute-care hospitals to implement ASP because improving use of ABAs is an important patient safety and public health issue as well as a national priority [11, 23]. Several benefits of such ASPs have been documented such as optimizing treatment of infections, reducing adverse effects associated with ABA use, improving quality of patient care, improving patient safety, increasing cure rates, reducing treatment failures, increasing correct prescribing and most importantly reduce ABR [24-29]. The core elements of ASPs suggested by the CDC are [1] leadership commitment [2], accountability [3], drug expertise [4], action [5], tracking [6], reporting [7] and, education [23].

Problem of ABR had to be confronted seriously: the innumerous initiatives and publications available in the literature is testimony that no intervention is entirely satisfactory in combating the problem. As long as ABAs are in use, ABR is an inevitable consequence.

"While it is self-evident that the use of antimicrobial drugs has imposed selective pressures on the emergence of resistant microbes, to attribute the development of resistance entirely to imprudent antimicrobial use is, a fallacy that reflects an alarming lack of respect for the incredible power of microbes" [30].

All what we can do is to delay the emergence and spread of ABR by implementing these initiatives.

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REVIEW ARTICLE

SLHPBA guidelines on the management of acute pancreatitis - a consensus document

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Acute pancreatitis continues to be one of the leading causes of hospital admission for 'acute abdomen' globally including Sri Lanka. The presentation and outcome spans a wide spectrum from those who present with a mild episode that requires a few days of hospitalisation to those who develop severe disease with multi-organ dysfunction, associated local infective complications with attendant morbidity and mortality.

Similar to elsewhere in the world, in Sri Lanka, acute pancreatitis is managed by specialists that include general surgeons, gastrointestinal surgeons, general physicians and gastrointestinal physicians. In addition, radiologists, microbiologists and critical care specialists play a key role in the overall care of these patients. The concept of centralised care in pancreatic disorders is yet to be established resulting in its overall level of care being somewhat heterogeneous.

Data regarding the incidence of acute pancreatitis and its outcomes in Sri Lanka is sparse except for a handful of small unpublished studies of limited patient numbers. Reports of adverse outcomes secondary to inappropriate practice, failure to refer to specialist centres when appropriate and the lack of infrastructure and facilities have been noted.

It is in this context that the Sri Lanka Hepato-Pancreato-Biliary Association (SLHPBA) sought to address the need to establish consensus guidelines to manage this important condition. In generating these guidelines, their suitability and applicability in the national health system was an important factor, since more than 80% of inpatient care is currently provided in the state health sector. The availability of resources at different levels of hospitals in terms of expertise, ancillary facilities including facilities for CT imaging, interventional radiological support and intensive care were considered when making recommendations.

These guidelines also include globally established terminology in relation to local complications of acute pancreatitis enabling all care givers to communicate via a universal language. Furthermore, this will facilitate the development of national databases and auditing of results with a view to improving quality of care and outcomes.

The scope of these guidelines is to provide evidence based recommendations for the medical and surgical management of patients with acute pancreatitis both in the acute and later phase of the disease.

The primary guideline working group consisted of members of the SLHPBA and the IHPBA (International Hepato-Pancreato-Biliary Association). Individuals from relevant specialities and professional organisations including the College of Surgeons of Sri Lanka, Sri Lanka Society of Gastroenterology, Sri Lanka College of Radiologist and Sri Lanka College of Microbiologists were involved in the final drafting of the guidelines.

Target users of the guidelines are all clinicians involved in the care of patients with acute pancreatitis.

The evidence and recommendations for these guidelines were derived from the following three documents:

1. IAP/APA Evidence-Based Guidelines for the Management of Acute Pancreatitis [1]
2. The New Revised Classification of Acute Pancreatitis 2012 [2]
3. American College of Gastroenterology Guideline: Management of Acute Pancreatitis [3]

The strength of recommendations and the levels of evidence for the Sri Lankan guidelines will mirror those of the above guidelines that have utilised the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system. Clinicians who wish to read further with regard to the level of evidence forming the basis of the guidelines and recommendations are directed to the quoted three references.

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SRI LANKA HEPATO-PANCREATO-BILIARY ASSOCIATION
NATIONAL GUIDELINES 2017
MANAGEMENT OF ACUTE PANCREATITIS

A) Diagnosis

Fulfilment of **2 out of 3** of the following criteria (usually **1 & 2):**

1. Central upper abdominal pain usually of acute onset often radiating to the back
2. Serum amylase or lipase activity >3 times the upper limit of normal
3. Characteristic features on cross-sectional (CT / MRI) abdominal imaging

Note:

I. Serum amylase and lipase are primarily of diagnostic value and not indicators of disease severity. Hence, repeat assays are not indicated once a diagnosis is established.

ii. Optimal timing for initial CT assessment, if required, is **at least 72 - 96 hours** after onset of symptoms.

However, indications for early abdominal CECT in AP include:

1. Uncertainty of diagnosis in terms of clinical presentation e.g. suspected visceral perforation
2. Equivocal biochemistry in the presence of typical clinical picture
3. Clinical deterioration despite optimal care within 48-72 hours of admission

B) Assessment of severity

It is recommended that severity may be assessed using one of the methods a) or b) given below:

a) Organ failure based on Modified Marshall Score

Mild AP

- No organ failure
- Lack of local or systemic complications

Moderate AP

- Organ failure that resolves within 48 hours (transient organ failure) and/or
- Local or systemic complications (sterile or infected) without persistent organ failure

Severe AP

- Persistent single or multiple organ failure (>48 hours)

Definition of organ failure

Table 1. Modified Marshall Score

A score **≥2** in any system defines the presence of organ failure

	0	1	2	3	4
Respiratory PaO_2/FiO_2	>400	301-400	201-300	101-200	≤100
Renal (serum creatinine) µmol/L	≤ 134	134 - 169	170 - 310	311 – 439	> 439
mg/dl	< 1.4	1.4 – 1.8	1.9 – 3.6	3.7 – 4.9	≥ 5
CVS SBP mmHg	> 90	< 90 fluid responsive	< 90 non responsive to fluid	<90 pH < 7.3	< 90 pH < 7.2

- Scoring patients with pre-existent CKD depends on the extent of deterioration over baseline renal function. Calculations for a baseline serum creatinine ≥134 mmol/L or 1.4 mg/dL are not available.
- SBP - off inotropic support

b) Severity based on systemic inflammatory response syndrome (SIRS)

SIRS is defined by the presence of **two (2) or more** of the following four (4) criteria:

(1) Temperature < 36 °C (96.8 °F) or >38 °C (100.4 °F)
(2) Heart rate >90 / min
(3) Respiratory rate >20 / min
(4)White blood cells <4000/mm^3, >12000/mm^3 or 10% band forms

Severe acute pancreatitis in indicated by SIRS at **admission** and persistent SIRS at **48 h**

Note:

Other indicators of severe AP at admission or 72 h

- CRP ≥**150** mg/dL

Local complications (see annexure for definitions)

1. Acute peripancreatic fluid collection (APFC)
2. Pancreatic pseudocyst
3. Acute necrotic collection (ANC)
4. Walled off necrosis (WON)
5. Gastric outlet obstruction
6. Splenic / portal vein thrombosis
7. Retroperitoneal haemorrhage
8. Pancreatic ascites
9. Pancreatico-pleural fistula

C) Initial assesment and risk stratification

1. Haemodynamic status should be assessed immediately upon presentation and resuscitative measures begun as needed
2. Baseline investigations on admission:

   FBC, CRP, BU, creatinine, electrolytes, AST / ALT, bilirubin, ALP

   ABG (in haemodynamically abnormal / oliguric / tachypnoeic patients)

3. **Ultrasonography** should be performed in all patients **within 24 hours** to evaluate the biliary tract for:
   - Gallstones
   - Common bile duct (CBD) calculi
   - Biliary tract dilatation

4. Risk stratification is required to
   - Predict outcome of AP
   - Determine those who require HDU / ICU care

5. A 3-dimensional approach to risk stratification is recommended:
   - Host risk factors (e.g. age, co-morbidity, body mass index)
   - Disease severity (mild / moderate / severe)
   - Response to initial therapy (clinical & biochemical)

6. Admission to an HDU or ICU is recommended in
   - Evolving or established organ failure (moderate – severe AP)
   - Elderly, multiple co-morbidities

D) Management

1. Initial fluid therapy

a. Aggressive hydration, defined as **5 - 10 ml/kg/h** of isotonic crystalloid solution should be provided to all patients, unless cardiovascular and/or renal co-morbidities exist. Early aggressive intravenous hydration is most beneficial the **first 12 – 24 h**, and may have little benefit beyond

b. In patients with severe volume depletion, manifest as hypotension and tachycardia, more rapid repletion (bolus) may be needed

c. Recommended fluid: **Hartmann** (Ringer's lactate) solution

d. Fluid therapy should be **goal directed** and **reassessed** at frequent intervals within 6 h of admission and for the next 24 – 48 h.

e. The goals of initial fluid therapy:
   - Heart rate < 120 bpm
   - MAP 65 - 85 mmHg
   - Urine output 0.5 – 1.0 ml / kg / hr
   - Haematocrit 35 – 40 %
   - Blood urea reduction

   Note: trends in parameters are important

2. Pain relief

Multimodal analgesic regimens are recommended
- Paracetamol – suppositories
- Opioids – Morphine IV / SC
- NSAIDs (caution in renal impairment)

3. Antibiotics

a. Routine use of prophylactic antibiotics in patients with mild, moderate or severe AP is **not** recommended

b. The use of antibiotics in patients with sterile necrosis to prevent the development of infected necrosis is **not** recommended

c. Routine administration of antifungal agents is **not** recommended

d. In patients with suspected infected necrosis, antibiotics known to penetrate pancreatic necrosis, such as carbapenems, quinolones, and metronidazole, may be useful in delaying or sometimes totally avoiding intervention, thus decreasing morbidity and mortality

e. Antibiotics should be given for an extra-pancreatic infection, such as cholangitis, catheter-acquired infections, bacteraemia, urinary tract infections, pneumonia

4. Nutrition

a. In mild AP, oral feeds can be started immediately if there is no significant pain, nausea and vomiting

b. In mild AP, initiation of feeding with a low-fat solid diet appears as safe as a clear liquid diet

c. In severe AP, nasogastric / jejunal **enteral nutrition is recommended** to prevent infectious complications

d. **Polymeric formulations are as effective** as elemental for-mulations for enteral nutrition in AP

e. Nasogastric and nasojejunal enteral feeding appear comparable in efficacy and safety

f. Parenteral nutrition is instituted in AP **only** if enteral (NG/NJ) feeding is not tolerated and fails to meet nutritional requirement

5. ERCP (endoscopic retrograde cholangio pancreaticography)

a. Patients with AP and
   - concurrent acute cholangitis or
   - biliary tract obstruction should undergo **urgent ERCP within 24 h** of admission

b. Pancreatic duct stents and / or post-procedure rectal NSAID suppositories should be utilized to prevent severe post-ERCP pancreatitis in high-risk patients

c. In unstable and if ERCP is not safely feasible, placement of a percutaneous transhepatic (PTC) biliary drainage tube should be considered

d. ERCP is **not** needed in most patients with gallstone pancreatitis who lack laboratory or imaging evidence of ongoing biliary obstruction

e. If choledocholithiasis is strongly suspected in the absence of cholangitis and/or jaundice, MRCP or endoscopic ultrasound (EUS) is recommended

6. Cholecystectomy

a. In patients with mild AP with gallstones, a laparoscopic cholecystectomy should be performed during the index admission **before discharge** to prevent a recurrence of AP

b. If a cholecystectomy cannot be done during the index admission it should be done **within 2 weeks** of discharge

c. In a patient with severe or necrotizing gallstone AP, in order to prevent infection, cholecystectomy is to be deferred until active inflammation (clinical & biochemical) subsides and fluid collections resolve or stabilize

7. Management of local complications

a. The presence of ***asymptomatic*** pseudocysts and pancreatic and/or extra-pancreatic necrosis do **NOT** warrant intervention, regardless of size, location, and/or extension

b. Indications for intervention (radiological / endoscopic / surgical) in **sterile** necrotizing AP are:

- Ongoing gastric outlet, intestinal, or biliary obstruction due to mass effect of WON (i.e. arbitrarily > 4 - 8weeks after onset of AP)
- Persistent symptoms (e.g. pain, 'persistent unwellness') in patients with WON without signs of infection (i.e. arbitrarily > 8 weeks after onset of AP)
- Disconnected duct syndrome (i.e. full transection of the pancreatic duct in the presence of pancreatic necrosis) with persisting symptomatic (e.g. pain, obstruction) collection(s) with necrosis without signs of infections (i.e. arbitrarily > 8 weeks after onset of AP)
- Ongoing organ failure for several weeks after the onset of AP, preferably after WON

c. Other indications for emergency surgery **without** concurrent necrosectomy

- Abdominal compartment syndrome
- Ongoing acute bleeding
- Bowel ischaemia

8. Diagnosis & treatment of infected necrosis

a. Infected necrosis should be considered in patients with pancreatic or peripancreatic necrosis who **deteriorate or fail to improve after 7 – 10 days** (2nd week onwards) of hospitalization.

b. It is diagnosed by:

- Clinical features of ongoing sepsis
- CECT – extraluminal gas in pancreatic or peri-pancreatic necrotic tissue
- Percutaneous FNA for microbiological analysis – **not recommended**

c. In **stable** patients with infected necrosis, surgical, radiological, and/or endoscopic drainage should be **delayed** preferably for **more than 4 weeks** to allow liquefaction of the contents and the development of a fibrous wall around the necrosis (walled-off necrosis)

d. In **symptomatic** patients with infected necrosis, **minimal access** methods (percutaneous / endoscopic transluminal) are preferred to open necrosectomy

e. Patients with

- extensive necrotizing acute pancreatitis
- who show no clinical signs of improvement following appropriate initial management
- who experience other complications
- should be managed in institutions that have on-site or access to therapeutic endoscopy, interventional radiology, surgeons and intensivists with expertise in dealing with severe acute pancreatitis.

9. Determination of aetiology

a. In the absence of gallstones and/or history of significant history of alcohol use, a detailed history should be obtained to look for aetiological factors

b. Serum triglyceride should be obtained and considered the aetiology if > 1,000 mg / dl

c. Serum ionised calcium if above normal should be investigated for primary hyperparathyroidism

d. In patients **>40 years**, a pancreatic **tumour** should be considered and a **CECT** performed

e. Patients with idiopathic pancreatitis should be referred to centres of expertise

f. Genetic testing may be considered in young patients (<30 years old) if no cause is evident and a family history of pancreatic disease is present

Definitions

Types of AP

1. Interstitial oedematous pancreatitis

Inflammation of pancreatic parenchyma and peri-pancreatic tissue, but without obvious tissue necrosis.

- Enhancement of the pancreatic parenchyma by contrast agent
- No evidence of peripancreatic necrosis (see below)

2. Necrotizing pancreatitis

- Inflammation with pancreatic parenchymal necrosis and/or peripancreatic necrosis.
- Areas of pancreatic parenchymal lacking by intravenous contrast agent and/or
- Findings of peripancreatic necrosis (see below—ANC and WON)

Local complications

1. Acute peripancreatic fluid collection (APFC)

Peripancreatic fluid with interstitial oedematous pancreatitis and no peripancreatic necrosis. This term applies to peripancreatic fluid seen within the *first 4 weeks* after the onset of interstitial oedematous pancreatitis.

- Homogeneous collection with fluid density adjacent to pancreas confined by normal
- peripancreatic fascial planes
- No recognizable wall encapsulating the collection
- Occurs only in interstitial oedematous pancreatitis

2. Pancreatic pseudocyst

Encapsulated fluid collection with minimal or no necrosis with a well-defined inflammatory wall usually outside the pancreas. This entity occurs *more than 4 weeks* after the onset of interstitial oedematous pancreatitis.

- Round or oval well circumscribed, homogeneous fluid collection
- No non-liquid component
- Well-defined wall
- Occurs after interstitial oedematous pancreatitis

3. Acute necrotic collection (ANC)

A collection of both fluid and necrosis associated with necrotizing pancreatitis involving the pancreatic parenchyma and/or the peripancreatic tissues

- Heterogeneous, non-liquid density of varying degrees
- No definable encapsulating wall
- Location: intrapancreatic and/or extrapancreatic
- Occurs in setting of acute necrotizing pancreatitis

4. Walled-off necrosis (WON)

A mature, encapsulated collection of pancreatic and/or peripancreatic necrosis with a well-defined inflammatory wall occurring *more than 4 weeks* after the onset of necrotizing pancreatitis.

- Heterogeneous liquid and non-liquid density with varying degrees of loculations
- Well-defined encapsulating wall
- Location: intrapancreatic and/or extrapancreatic
- Occurs only in setting of necrotizing pancreatitis

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Acknowledgment

The primary guideline working group consisted of members of the SLHPBA and the IHPBA (International Hepato - Pancreato - Biliary Association). Individuals from relevant specialities and professional organisations including the College of Surgeons of Sri Lanka, Sri Lanka Society of Gastroenterology, Sri Lanka College of Radiologist and Sri Lanka College of Microbiologists were involved in the final drafting of the guidelines.

TECHNICAL NOTE

Pancreatico-duodenectomy with long segment portal vein resection and reconstruction with left renal vein autologous graft

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Key words: Pancreatic cancer; pancreatico-duodenectomy; portal vein resection; portal vein reconstruction; autologous left renal vein graft

Introduction

Management paradigm of pancreatic cancer (PC) is evolving, yet the only hope of cure is complete resection with negative margin. In minority of cases negative margin during pancreatico-duodenectomy (PD) can be achieved only with portal vein resection (PVR) [1]. Long segment PVR has to be reconstructed using a conduit for which left renal vein autologous graft (LRAG) is a viable option [2, 3].

To date there are no reported cases of major PV reconstruction in Sri Lanka. Hence we report our first experience of PVR and reconstruction using LRAG.

Case presentation

A 47 year old male was investigated for painless obstructive jaundice. Preoperative cross sectional imaging revealed pancreatic head mass with involvement of PV. PD with possible PVR was planned.

Intra operatively hard pancreatic head mass infiltrating about 2cm segment of PV at its origin was noted (Figure 1). Following standard dissection pancreas was transected at the neck. Complete uncinate process dissection done and replaced right hepatic artery was appreciated and preserved (Figure 1). Splenic vein was ligated. After fully mobilizing the liver, it was decided that end to end anastomosis of PV was not possible due to longer segment involvement. Considering the normal renal function LRAG was planned.

Kocherization was extended. Left renal vein was exposed slung and traced up to left adrenal vein (Figure 2). Left renal vein was controlled with two clamps and harvested preserving the adrenal vein. PV reconstruction was completed with LRAG using 5/0 prolene (Figure 3). Postoperative good PV flow was identified. Patient made an uneventful recovery.

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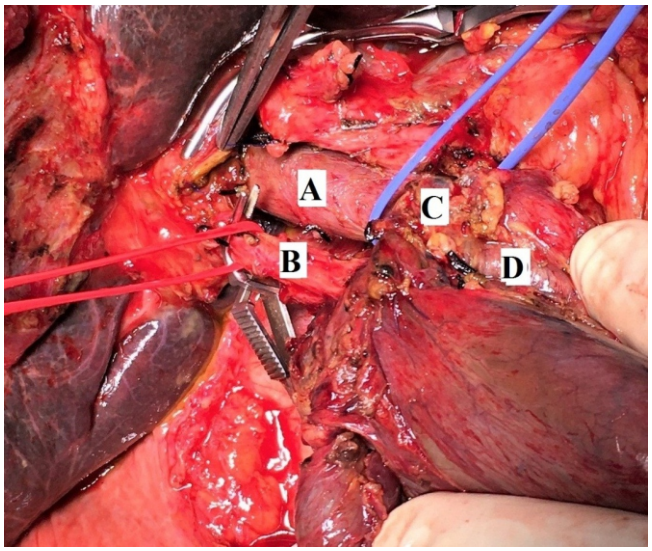

Figure 1. A - Portal vein, B - Replaced right hepatic artery, C - Tumour infiltrating the portal vein, D - Superior mesenteric vein

Discussion

Surgical resection is the only treatment that offers cure for pancreatic cancer. At times portal vein resection increases the resectability with negative margins, hence chances of cure [1, 4]. First reported case of major venous resection by Moore in 1951 . However PVR are exceptional even in high volume hepatobiliary centres [3]. Many studies including a recent meta-analysis proved PVR has no added morbidity and mortality [1, 4, 5, 6].

There are many options for PV reconstruction. Apart from cadaveric grafts, other options such as autologous jugular, left renal, femoral and external iliac veins grafts and synthetic grafts are reportedly used [2, 3]. By preserving the adrenal vein LRAG can be successfully used without remarkable renal dysfunctions [2].

Careful case selection and ability of major venous reconstruction should be the goal in units that treat PC more frequently.

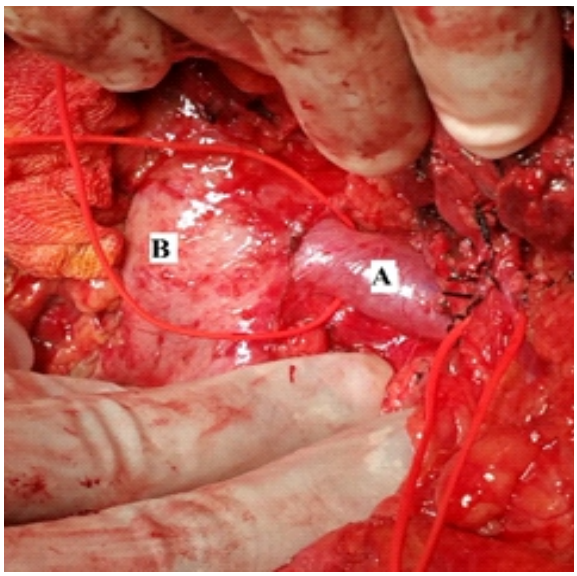

Figure 2. A - Left renal vein, B - IVC

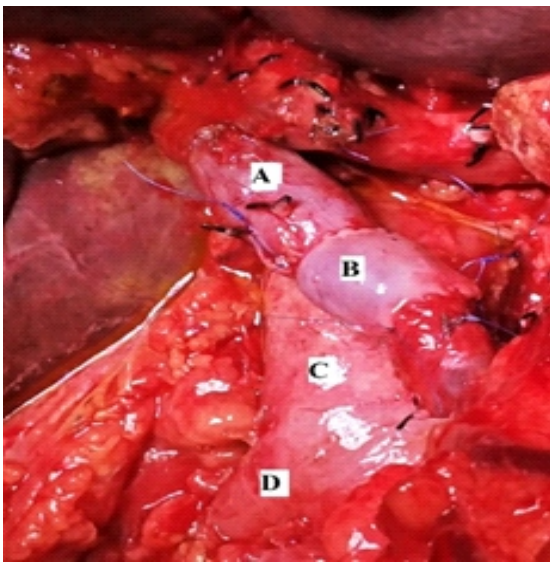

Figure 3. A - Portal vein, B - Autologous left renal vein graft, C - IVC, D - Right renal vein

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BRIEF REPORT

Incidence of post-operative hypocalcaemia after thyroidectomy - a retrospective study

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Key words: Thyroidectomy; post-operative; serum calcium level

Abstract

Introduction

Post-operative hypocalcaemia following thyroidectomy can lead to distressing symptoms and increase the period of hospitalization. Iatrogenic injury to parathyroid glands is the primary cause for hypocalcaemia.

Aim

This study aims to describe the incidence of postoperative hypocalcaemia and its demographic distribution.

Method

A retrospective analysis was made in 240 consecutive patients who had undergone total thyroidectomy in the professorial surgical unit, Teaching Hospital Jaffna. The post-operative calcium level, symptoms and signs of hypocalcaemia were considered and correlated with their demographic details and histology report of the specimen.

Results

The overall incidence of hypocalcaemia was 10.83% (n=26). Among them, 96.15% (n=25) had transient hypocalcaemia and 88.46% had symptomatic hypocalcaemia (n=23) with biochemical evidence of hypocalcaemia. The rate of inadvertent parathyroidectomy was 6.25%.

Conclusion

Hypocalcaemia is common in the first three days of postoperative period and most of the hypocalcaemic events are transient.

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Introduction

Thyroidectomy is a common operation in Sri Lanka, including the northern region. The incidence of postoperative hypocalcaemia has not been analysed in northern region. The aim of this study is to describe the incidence of hypocalcaemia after total thyroidectomy and its demographic distribution.

Post-operative hypocalcaemia is frequently seen within the first few days after total thyroidectomy [1, 2]. It is most often transient and may indicate iatrogenic injury to parathyroid gland [1, 2]. The incidence of inadvertent parathyroidectomy was reported to be 12-16.4% in the literature. The risk factors include total thyroidectomy, extra thyroidal extension and thyroiditis [1, 2, 3]. The response to calcium replacement therapy for transient hypocalcaemia after thyroidectomy can be seen in a few days to weeks [4]. The persistent hypocalcaemia after 6 months of thyroidectomy is considered permanent hypocalcaemia [5]. The incidence of permanent hypocalcaemia is less than 1-2 % [6, 7].

Hypocalcaemia may be asymptomatic or symptomatic depending on the serum calcium level. Chvostek's and Trousseau's signs, paraesthesia and muscle spasm are clinical manifestations of hypocalcaemia [8].

Materials and Methods

A retrospective analysis was carried out in the professorial surgical unit of Teaching Hospital Jaffna from 1st January 2011 to 1st July 2016. Data of consecutive patients who underwent thyroidectomy during this period were collected. The inclusion criteria were patients who underwent total, near total or completion thyroidectomy. Exclusion criteria were previous history of parathyroid diseases, renal insufficiency, patients with preoperative calcium replacement therapy and abnormal pre-operative calcium level. Data collected include age, sex, indication for thyroidectomy, pre and post-operative serum calcium level, the presence of postoperative symptoms and signs of hypocalcaemia and the histology report of the specimen. Serum calcium levels in these patients were monitored preoperatively and postoperatively daily up to day six and then weekly up to six weeks. Thereafter serum calcium level was monitored monthly in patients whose calcium levels were low after six weeks. Hypocalcaemia was defined as the corrected calcium level below 8.5 mg/dl. Permanent

hypocalcaemia was defined as persistent hypocalcaemia after 6 months of thyroidectomy.

Data were entered and analysed using the statistical package for social science (SPSS) and the results were expressed as a percentage, mean, standard deviation and ratio. This study is approved by the Ethical Review Committee, Faculty of Medicine, University of Jaffna.

Result

A total of 240 patients were included in our study. The number of patients who underwent thyroidectomy and their diagnosis is listed in table 1.

All patients had pre-operative normal calcium levels. The overall incidence of hypocalcaemia was 10.83% (n=26). Symptomatic hypocalcaemia was observed in 88.46% (n=23) of patients with evidence of biochemical hypocalcaemia. The details of frequency of hypocalcaemia, the age and gender distribution are indicated in tables 2 and 3.

The onset of hypocalcaemia after thyroidectomy is indicated in table 4. The hypocalcaemia in these patients was managed with calcium supplements and Vitamin D. Transient hypocalcaemia was noted in 25 patients and one patient suffered from permanent hypocalcaemia. The time of recovery for patients with transient hypocalcaemia is shown in table 5.

The histopathology reports revealed accidental removal of parathyroid glands in 15 patients (6.25%).Of these 15 patients, 4 developed hypocalcaemia. Among these 4 patients two parathyroid glands have been removed in 3 patients and one removed in 1 patient. Permanent hypocalcaemia was noted in one patient after thyroidectomy with accidental removal of 2 parathyroid glands. Nine patients with accidental removal of one parathyroid gland and 2 patients with removal of two parathyroid glands did not develop hypocalcaemia.

Discussion

The overall incidence of postoperative hypocalcaemia in this study is 10.8%. The incidence of hypocalcaemia was 10 – 46 % noted in most of the literatures [5, 7, 9]. Transient hypocalcaemia is a common occurrence after total thyroidectomy [1, 10, 11]. In this study, 96.15% of hypocalcaemia cases are transient. A patient undergoing total thyroidectomy risks vascular injury to the four parathyroid glands due to the requirement for bilateral dissection [12]. It is recommended that with careful dissection of the blood supply of the

Table 1: Diagnosis of patients underwent thyroidectomy

Diagnosis	Number of patients
Multi nodular goitre (MNG)	77
Graves	28
Toxic MNG	26
Thyroid Malignancy (Solitary)	58
Thyroid Malignancy (MNG)	38
Recurrent Goitre	13

Table 2: Age Distribution of the patients and frequency of hypocalcaemia

Age Distribution	Number of Patients	Percentage	Number of patients who developed hypocalcaemia	Percentage
<19 years	75	31.3%	5	6.66%
20 – 49 years	110	45.8%	14	12.72%
>50 years	55	22.9%	7	12.72%

Table 3: Gender distribution of patients and frequency of hypocalcaemia

Sex	Number of patients	Percentage	Number of Patients who developed Hypocalcaemia	Percentage
Male	43	17.9%	5	11.62%
Female	197	82.1%	21	10.65%

Table 4: Time of onset of biochemical hypocalcaemia

Post-Operative Day	D1	D2	D3	D4	D5
Number of patients	3	12	9	1	1
Percentage	1.25%	5%	3.75%	0.4%	0.4%

Table 5: Time of recovery of patients with hypocalcaemia.

Time of recovery	Number of Patients with transient hypocalcaemia
First week	21
Second week	4

parathyroid glands they can be spared. Ligation of the inferior thyroid artery close to the thyroid capsule is better in preserving the integrity of the parathyroid gland than ligating close to its origin. Identification of parathyroid gland during surgery is an important factor to prevent post-operative hypocalcaemia as described in various literature. Accidental removal of parathyroid gland was observed as 6.25% in this study as compared to other studies where it was 17.7% of the patients undergoing total thyroidectomy [6]. It is reported that identification and preservation of less than three parathyroid glands are associated with permanent hypocalcaemia according to the literatures [13]. The removal of two parathyroid glands leads to permanent hypocalcaemia in our study. Most of the patients who developed hypocalcaemia were observed within first three days, which correlates with other studies [6].

Conclusion

Hypocalcaemia commonly occurs during the first three days of postoperative period. Most of the hypocalcaemic incidences in post-thyroidectomy are transient in nature and will recover within a period of one week.

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CASE REPORT

Bilateral atraumatic acute anterior compartment syndrome of the legs with rhabdomyolysis and acute kidney injury

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Key words: compartment syndrome; fasciotomy; rhabdomyolysis; acute kidney injury; exercise

Introduction

Acute Compartment Syndrome (ACS) occurs within closed fascial compartments where the intra-compartmental pressure increases progressively, resulting in reduced tissue perfusion within the compartment [1]. The increase in interstitial pressure eventually overcomes the capillary perfusion pressure, resulting in a state of tissue hypoxia. Once the interstitial pressure rises >30 mmHg or within 25 mmHg of the diastolic pressure, muscle ischemia begins [2]. Hypoxic injury releases metabolites that trigger further inflammation and further increase in compartmental pressure with progressive tissue injury. While ACS can occur in numerous locations including abdomen, thoracic cavity and brain, the commonest form is seen in the muscular compartments of the limbs, primarily the lower limbs.

Lower limb compartment syndrome can be either acute or chronic. ACS is usually seen after trauma including fractures, crush injury, burns, inadvertent intra-arterial injections or severe infections. It can also occur following reperfusion of an ischaemic limb. The annual incidence of post-traumatic ACS has been reported to be as high as 3 per 100,000 [3]. Chronic compartment syndrome (CCS) is less common, usually seen in young athletes or military personnel after strenuous exercise. Atraumatic post-exertional ACS is seen less frequently, usually unilateral and in an individual with a preceding history of CCS. The occurrence of bilateral atraumatic ACS without a history of CCS is extremely rare with only a handful of reported cases. This report describes such a patient with atraumatic bilateral ACS complicated with rhabdomyolysis and acute kidney injury (AKI).

Case presentation

A 34-year old man presented to the Emergency Department with a history of painful swelling in both legs for 8 days. He is a computer professional working overseas and had a relatively sedentary life style. He had no known co-morbidities, was a non-smoker and did not use recreational drugs. He had no preceding history of CCS. One day after work he had done extended jogging and came home with some unusual discomfort in the legs. He tried simple home remedies but the symptoms rapidly deteriorated. At the local hospital, he was treated for suspected cellulitis due to the red discolouration on his legs. His condition worsened with progressive pain, swelling and weakness of the legs. By day-03, he noticed dark brown discolouration of his urine. Due to his progressive deterioration, he was brought back to Sri Lanka and immediately admitted to hospital.

On initial assessment, he was febrile (37.4 C) and in severe pain. The pulse rate was 96/min with a respiratory rate of 20/min. The blood pressure was 110/65 mmHg. There was marked swelling in both legs below the knee, with a well demarcated reddish discolouration corresponding to the anterior compartments (Figure 1). This region was severely tender and extremely firm compared to the rest of the calf.

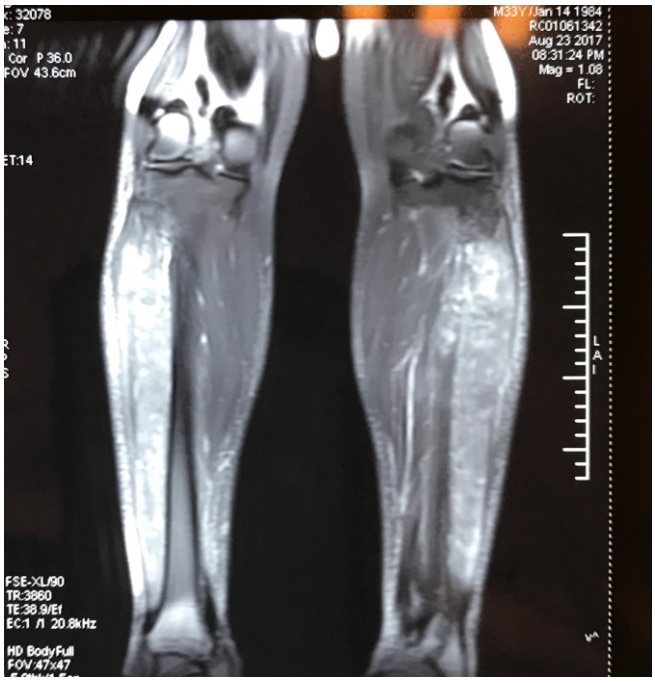

Figure 1. MRI scan showing bilateral anterior compartment oedema and ischaemic damage. Posterior compartments are spared.

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While the posterior tibial pulses were normal, the anterior tibial pulse was not palpable on either side. Doppler assessment showed a triphasic signal over the posterior tibial and a monophasic signal over the anterior tibial artery. He had a complete bilateral foot drop with significant paraesthesia around the dorsum of the foot. He had an indwelling urinary catheter and the urine was dark brown.

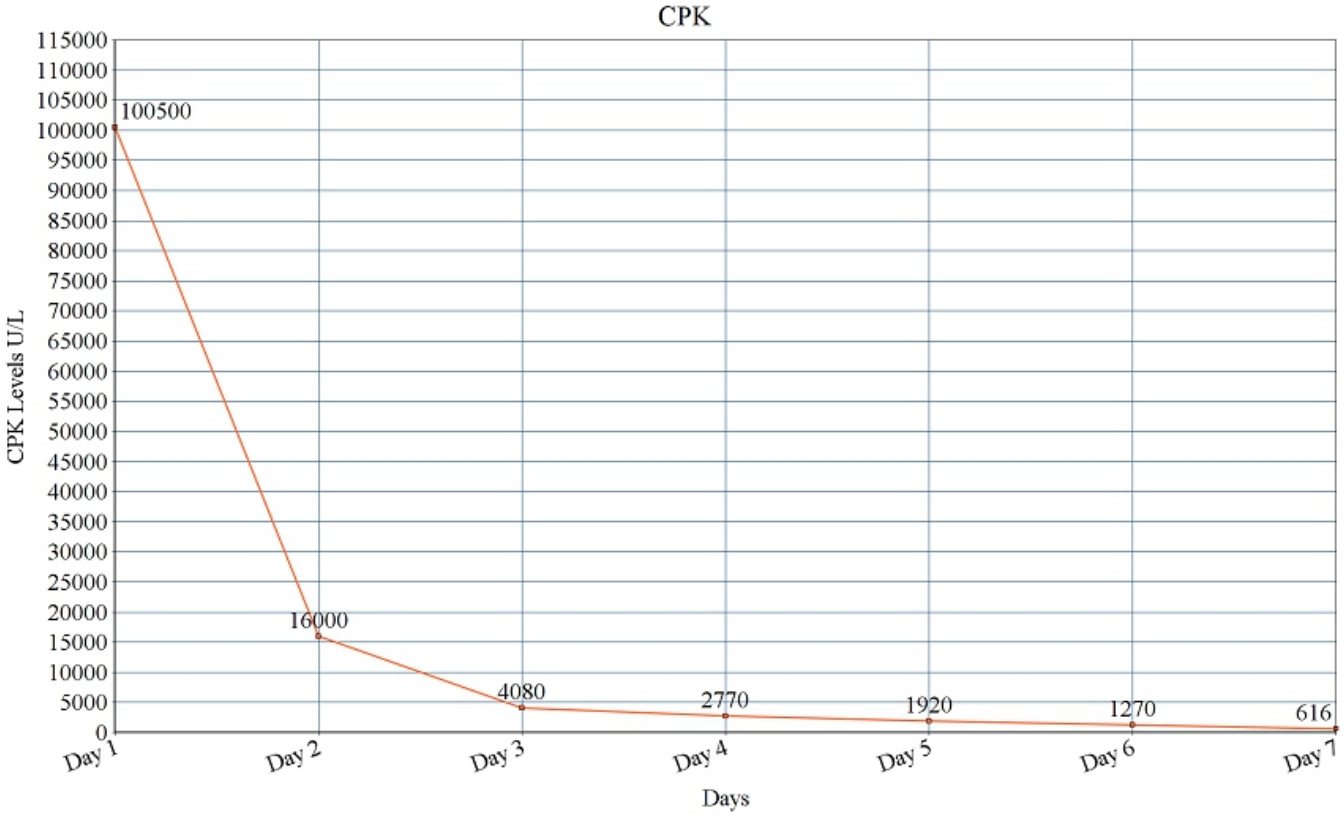
Initial blood biochemistry results were; white cell count – 19.8× 109 /l, haemoglobin - 14.7 g/dl, serum creatinine - 187 mol/l and serum creatine phospokinase (CPK) – 100,500 U/l. Urine for myoglobin was strongly positive.

A clinical diagnosis of bilateral ACS with rhabdomyolysis and AKI was made. An urgent MRI scan was done to assess the degree of muscle involvement and showed isolated whitening in bilateral anterior compartments (Figure 2). Compartmental pressure measurements were not pursued due to the overwhelming clinical evidence in favour of the diagnosis.

The condition, therapeutic options and potential outcomes were discussed with the patient and his spouse. Emergency bilateral decompressive fasciotomy was performed, with a full length anterior compartment releasing incision and a limited lateral incision to release the other three compartments. Anterior compartment muscles were non-viable on both legs, being pale brown with no capillary bleeding and no contractility. All other compartments showed normal viability. The wounds were left open with soft dressings. Prophylactic intravenous antibiotics (meropenam 500 mg 8 hourly) were continued peri-operatively. Furthermore, aggressive fluid resuscitation was done along with urinary alkalinization (sodium bicarbonate) and forced diuresis (mannitol) to minimize the effects of AKI.

Figure 2. Lateral fasciotomy of the left calf showing

The immediate post-operative recovery was uncomplicated with dramatic improvement in pain, swelling and degree of paraesthesia. On post-operative day-03, he was afebrile and the urine colour had returned to normal. Urine for myoglobin was negative at this stage. The serum creatinine returned to normal limits by day-03. There was dramatic improvement in the serum CPK levels over the next few days (Graph 1). Active physiotherapy was started and he was mobilized after day-03. A negative pressure vacuum system was applied to



Graph 1. CPK level decline after fasciotomy

the fasciotomy wounds on day-05. By day-09, he was pain-free and able to walk with support. He was discharged at this time with continued physiotherapy and oral antibiotics. The negative pressure dressing was changed at weekly intervals.

Approximately 3 weeks after the fasciotomy, his wounds showed good granulation and no infection. The negative pressure dressing was removed and non-viable tibilais anterior muscle was excised. A split skin grafting was performed and wounds were closed. At 4 weeks follow up, he remains independently mobile. Although some degree of foot drop remains, with sustained physiotherapy he remains minimally disabled and is able to walk and climb stairs independently.

Discussion

The earliest description of atraumatic exercise induced ACS dates back to 1954, where Dr. Edward Wilson described his own symptoms during an Antarctic expedition [4]. Subsequently, several reports appeared that described exercise induced ACS causing muscle necrosis, usually in soldiers or athletes, termed 'march myositis' [5,6]. However, exercise induced bilateral ACS is extremely rare with only a handful of reported cases [7].

In the absence of a preceding CCS or significant local trauma, the early presentation of ACS can often be misleading, resulting in significant delay in diagnosis. ACS is primarily a clinical diagnosis and a high index of suspicion is required to avoid catastrophic complications. Severe unrelenting pain with tense muscle compartments should always raise the suspicion of ACS. The associated rise in serum CPK is a significant determinant in the early diagnosis [8]. Treatment involves immediate and complete fasciotomy and compartment decompression. Although early stages ACS may be managed conservatively with compartmental pressure monitoring, advanced ACS such as in this patient requires immediate fasciotomy. Supportive care is needed to avoid secondary infection and minimize effects of rhabdomyolysis induced AKI. Once stabilized, early physiotherapy and mobilization can minimize long-term disability. It requires a team approach with surgeons, nephrologists, medical intensivists, physiotherapists and dedicated nursing staff.

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Learning Points:

- Anterior compartment syndrome can occur without a significant history of trauma.
- A high index of suspicion is required in cases of unexplained pain and swelling confined to one compartment.
- Accurate clinical diagnosis is the cornerstone in management.
- Unnecessary delay in diagnosis can have devastating consequences including renal damage, septicaemia and death.

CASE REPORT

Transthoracic oesophagotomy in managing impacted foreign body at lower oesophagus

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Key words: Transthoracic oesophagotomy; oesophageal foreign body

Introduction

Accidental ingestion of foreign bodies is very common in paediatric and elderly patients. In elderly it is commonly seen in patients with poor sensory perception and psychiatric disorders. Ingestion of dental appliances is the commonest cause seen in normal adults. Cervical oesophagus is the commonest site of impaction followed by mid and lower oesophagus. Most of these foreign bodies don't require a surgical intervention and will pass through the gastro-intestinal tract without a major sequel. Out of these 10-20% may require endoscopic removal and nearly 1% will require formal thoracoscopic or open surgical intervention. Here we present a case of removal of dental prosthesis impacted in lower oesophagus via transthoracic oesophagotomy.

Case presentation

A 54yr old female presented with dysphagia and odynophagia for 1 month following an ingestion of an upper dental prosthesis. With progressive symptoms patient presented to E.N.T department and subsequently attempted endoscopic removal via rigid oesophagoscopy. Patient was referred to thoracic surgical unit following failed endoscopic procedure and patient was planned for thoracotomy and oesophagotomy followed by primary repair.

Prior to surgery patient underwent orogastro-duodenoscopy which revealed the foreign body at 34cm form the incisor tooth covered with mucosa and granulation tissue incorporating it to oesophageal wall. The gastro oesophageal junction was at 38cm from incisors. On contrast enhanced CT imaging of thorax there were no features of oesophageal perforation and site of impaction couldn't be seen radiologically. Patient underwent left sided postero lateral thoracotomy via 8th intercostal space and there were no features of oesophageal perforation. On entry to the thoracic cavity an intercostal muscle flap was harvested based on posterior intercostal arteries. On palpation site of impaction identified and it was retrieved via longitudinal ophagotomy done in between two stay sutures. Oesophagotomy repaired with interrupted 3 0 PGA sutures in 2 layers and reinforced with an Intercostal muscle flap (Figure 1). Her post-operative period was uneventful with a period of 7 days of parenteral feeding and subsequently established on oral feeding after confirmation of no anastomosis leak clinically and contrast study (Figure 2). Patient was discharged on post op day 10 to be followed up at the clinic in 6 weeks.

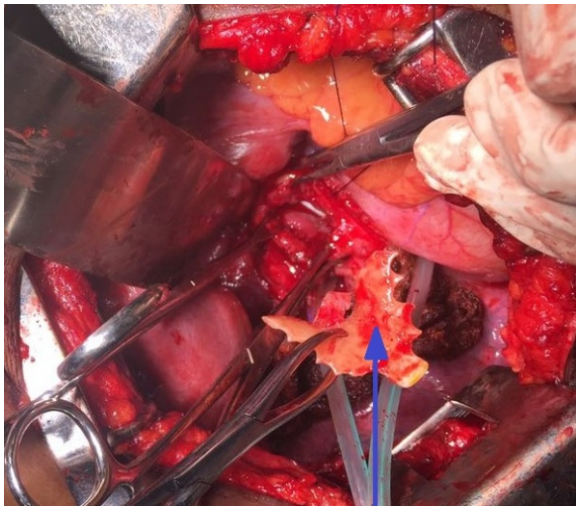

Figure 1. Retreval of foreign body via esophagotomy

Figure 2. Normal Oral contrast study

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Discussion

With the rising population of elderly people the use of dental prosthesis is high in number. This will result in increased chance of accidental ingestion of dental prosthesis. Depending on the size, shape, consistency, material and nature of the edges will determine the fate of the ingested prosthesis, especially the large ones with spiky edges require formal surgical intervention. Patient may present with wide array of clinical presentations ranging from dysphagia and odynophagia to life threatening complications. Oesophageal perforations along with empyema, mediastinitis and aortoesophageal fistula requires prompt diagnosis and treatment to reduce mortality associated with it. Patients presenting with late onset symptoms has the highest chance of perforation and associated complications.

Detailed clinical history along with radiological investigations and upper GI endoscopy will reveal the site and the nature of the substance which is ingested. This is a challenging process in children and elderly who cannot give a reliable history.

Endoscopic retrieval plays a major role as a minimally invasive method in dealing with foreign bodies in the oesophagus. This is more favourable in early presentation where there is less incorporation of the foreign body to oesophageal wall. Once the foreign body is incorporated to the oesophageal wall it requires formal thoracoscopic or thoracotomy approach to explore the site proceeded with oesophagomyotomy. Depending on the degree of contamination and nature of the oesophageal wall most of the time it is possible to proceed with primary suturing of the esophagotomy. As a method of reinforcing the anastomotic site an intercostal or pleural flap can be used. In patients presenting with empyema and mediastinitis removal of the septic focus along with discontinuation of the oesophagus via cervical oesophagostomy and feeding jejunostomy is advisable as a damage control approach.

Based on the published data oesophagotomy via thoracotomy and thoracoscopic approaches are safe procedures in managing delayed presentations of foreign body impacted in the oesophagus. Rigid or flexible Endoscopy plays a major role in early presentations. Patient should be routinely followed at clinics to detect post oesophagotomy stricture formation which may require dilatation later.

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Learning Points:

- In early presentations endoscopic retrieval plays a major role as a minimally invasive method in dealing with foreign bodies in the oesophagus.
- Esophagotomy via thoracotomy and thoracoscopic approaches are safe procedures in managing delayed presentations of foreign bodies impacted in the oesophagus.

CASE REPORT

An intussuscepting unusual tumour of small bowel: a metastasis from renal cell carcinoma ten years after the primary

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Keywords: renal cell carcinoma; intussusception; anaemia

Introduction

Renal cell carcinoma (RCC) is the third commonest urological malignancy. It is known to metastasize to any organ in the body. While its common sites to metastasize include lung, liver, bone and brain, small bowel involvement is very rare. We hereby report a case of a metastatic deposit in small bowel causing intussusception and chronic blood loss ten years after resection of the primary. There are less than ten such cases reported in the literature according to the authors' knowledge.

Case presentation

A 77 year old woman was investigated for symptomatic hypochromic microcytic anaemia. She had a laparoscopic radical nephrectomy in 2005 for localized (T2aN0M0) renal cell carcinoma of her right kidney of which the grade was 4 (Fuhrman). She had been free of recurrent disease in the interim.

On presentation, she had noticed some weight loss but had no symptom to point towards a focus of chronic blood loss. Her examination was unremarkable. Both gastroscopy and colonscopy were normal but stools for occult blood were positive. CT scan of abdomen revealed an intussusception in the left iliac fossa although a tumour was not clearly identified (Figure. 1).

She was discussed at the colorectal multidisciplinary meeting and was scheduled for an elective laparotomy. At surgery she had a tumour of the mid small bowel with intussusception and associated multiple lymph nodes in the mesentery. A segmental resection with removal of mesenteric lymph nodes was done with end to end anastomosis. Her recovery was uneventful.

Macroscopic examination revealed a 40 x 40 mm polypoidal tumour in the lumen of small bowel acting as a lead point for

Figure 1. CT scan showing the intussuception in the left iliac fossa

intussusception.

Microscopic examination revealed tumour cells with extensive hemosiderin deposition, varying from acinar pattern to more solid areas morphologically not typical of an intestinal primary.

Immunohistochemistry confirmed that it was a metastatic deposit from RCC which was invading the submucosa but not beyond. Resection margins and all mesenteric lymph nodes were clear. To this date she has had a disease free period of one year including a normal CT scan at one year.

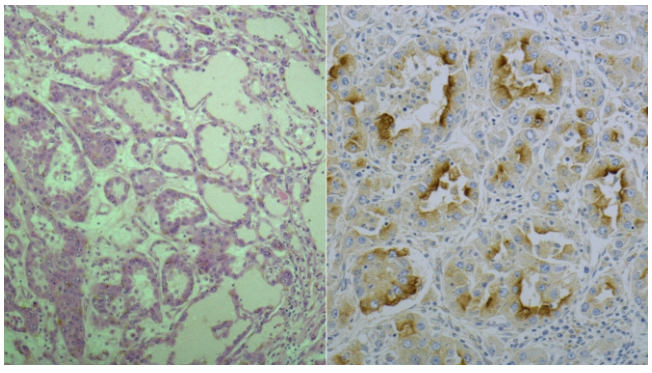

Figure 2. H and E Staining at 40 x (Left) and Immunohistochemical stain(Carbonic anhydrase IX) specific for RCC at 40x (Right)

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Discussion

Small bowel metastases from RCC are rare and are usually solitary [1-3]. The deposits may on occasion may be multiple [4]. The interval between primary treatment and diagnosis of small bowel metastases has been reported up to 20 years [3-5].

Most such cases have been presented with small bowel obstruction due to intussusception [1-3]. Frank or occult gastrointestinal bleeding has been seen in some cases [4].

CT scan has been the diagnostic tool in this case. This can potentially be negative especially if the lesions are small and there is no intussusception at the point of imaging. Capsular endoscopy has been useful in some of the cases described in literature in identifying subtle metastatic polyps of RCC [5]. Intra-operative endoscopic polypectomy has been used to excise small polyps in one case [4].

As in this case most patients in literature have been managed with a surgical resection of the affected segment of bowel, in some cases undertaken laparoscopically. Although there is enough evidence on efficacy of immune therapy and targeted therapy in metastatic renal cell cancer, evidence is scarce on its use following metastatectomy of such lesions as in this case.

Conclusion

RCC spread is via the hematogenous route and may therefore involve many sites including the small bowel. It should be suspected when a patient presents with occult blood loss with a history of RCC irrespective of the timing of primary. Metastatectomy of such deposits helps to palliate symptoms.

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Learning Points:

- Metastasis of renal cell carcinoma to small bowel is a very rare disease entity.
- Surgeons, physicians and radiologists need to be aware of this rare disease to accurately diagnose these patients.
- There is no management guidelines found and treatment is based on expertise and the scarce experience.

CASE REPORT

De novo papillary carcinoma in a thyroglossal duct cyst

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Keywords: Thyroglossal duct cyst; papillary carcinoma; thyroidectomy

Introduction

Thyroglossal duct cysts (TGDC) account for 70% of congenital neck masses1. Majority (70%) present during childhood and 7% in adulthood2. Only 1% of thyroid carcinomas develop in a TGDC3. A TGDC presents as an enlarging painless anterior neck mass in children or young adults, and is usually a clinical diagnosis. It is essentially impossible to clinically differentiate thyroglossal duct carcinoma from benign TGDC. A preoperative diagnosis may be suggested by ultrasound guided fine needle aspiration cytology. It is essential to differentiate primary papillary carcinoma in a TGDC from a metastatic papillary carcinoma of thyroid.

Case presentation

A 23 year old girl presented with a painless lump over the anterior neck for one month. The lump was gradually enlarging in size with no recent rapid enlargement. She had no local pressure symptoms such as difficulty in breathing or swallowing. There were no symptoms suggestive of hyper or hypothyroidism. Her past medical history was unremarkable with no adverse drug reactions or allergies. There was no family history of thyroid malignancies.

She was not pale or icteric. There was a non-tender firm midline lump located just above the hyoid bone. It was 2cm in diameter, spherical and smooth with well-defined edges. It was fluctuant but not transilluminable. Lump moved up with swallowing and also on protrusion of the tongue while stabilizing the jaw. Overlying skin was normal. No cervical lymphadenopathy or palpable thyroid nodules. The base of the tongue showed no ectopic thyroid tissue. No features of hyper or hypothyroidism. The other systems were normal.

Diagnosis and management

Ultrasound (USS) of the neck revealed a suprahyoid thyroglossal cyst and a sub-centimetre solitary thyroid nodule (STN) in the right lobe with no cervical lymphadenopathy. FNAC of the TGDC showed a benign cystic neoplasm. US guided FNAC of the right thyroid nodule was performed to exclude a primary papillary carcinoma of the thyroid which only revealed benign cells. Thyroid functions were normal.

A Sistrunk operation was done. Histology of the TGDC revealed a papillary carcinoma confirmed by immunohisto-chemical studies as CTF1 nuclear and CK19 positivity in cells lining the papillae.

A Total Thyroidectomy was performed following an oncological consultation to obtain a definitive tissue diagnosis of the thyroid nodule and to facilitate adjuvant treatment.

Histology of the thyroid nodule was of a papillomatous focus likely to be hyperplastic and rest of the gland normal. Immunostains were done on the suspicious focus and CK19 was negative confirming a benign lesion. Patient is currently on Thyroxine and is regularly followed up at our clinic and the oncology clinic.

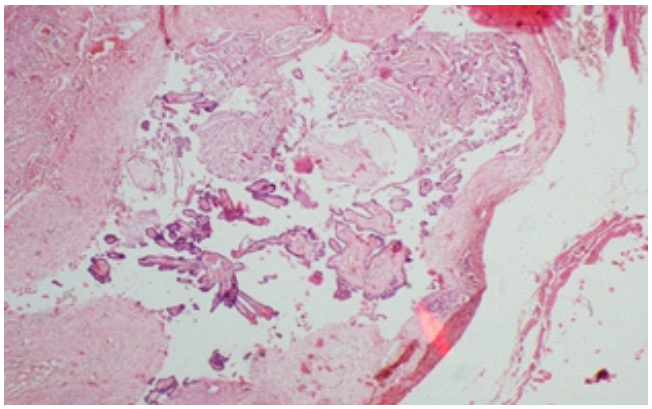

Figure 1. H&E Section of TGDC showing papillary proliferation with minimal nuclear changes suspicious of papillary carcinoma.

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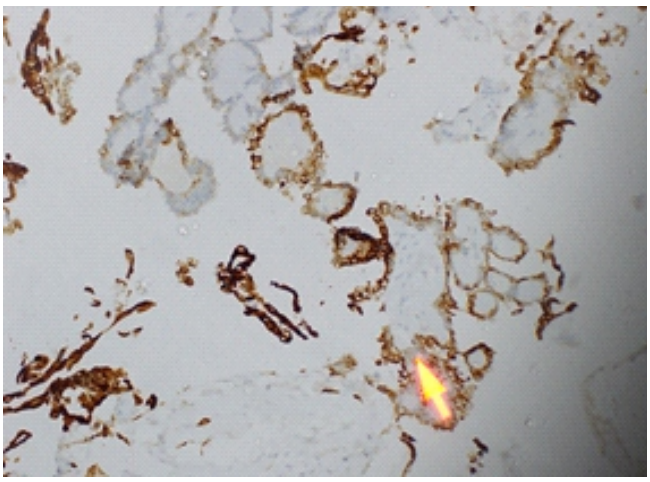

Figure 2. Immunohistochemical section of TGDC showing CTF1 nuclear positivity & CK19 diffuse membrane positivity in the cells lining the papillae confirming papillary carcinoma arising in a TGDC.

Discussion

TGDCs are the commonest developmental anomaly of the thyroid. However TGD carcinomas are very rare, with the majority arising from thyroid remnants4. Papillary carcinoma is the most common type (94%) with less than 5% squamous cell in origin5. The aetiology is uncertain. Two theories exist to explain the origin of TGD carcinomas. One is the de novo theory of origin of papillary carcinoma from a TGDC where the thyroid will be normal as in this case study. Secondly the metastatic spread from an occult primary papillary carcinoma of the thyroid due to its multifocal nature. Multifocal growth is common in papillary thyroglossal carcinomas, with a second lesion present in 10% of cases. Total thyroidectomy should be considered for differentiated thyroid malignancy in a thyroglossal cyst. Conservative management is only advocated in females less than 40 years of age, no capsular invasion and tumour size less than 1cm. Large tumours require total thyroidectomy followed by radioiodine ablation plus TSH suppression as for a thyroid malignancy. In the presence of positive cervical lymph nodes a cervical block dissection is indicated. On the other hand no additional treatment is needed apart from Sistrunk procedure for squamous cell origin of TGD carcinoma.

Conclusion

De novo papillary carcinoma in a TGDC is rare. Often it is an incidental diagnosis after surgical resection. Total thyroidectomy would be indicated in some patients.

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Learning Points:

- Surgically excised Thyroglossal duct cysts should always be sent for histopathology.
- It is essential to differentiate primary papillary carcinoma in a TGDC from a metastatic papillary carcinoma of thyroid.

SELECTED ABSTRACT

Sign of the Zodiac as a Predictor of Survival for Recipients of an Allogeneic Stem Cell Transplant for Chronic Myeloid Leukaemia (CML): An Artificial Association

R.M. Szydlo, I. Gabriel, E. Olavarria, J. Apperley

Transplant Proc. 2010 Oct;42(8):3312-5
doi: 10.1016/j.transproceed.2010.07.036

Abstract

Background

Astrological or Zodiac (star) sign has been shown to be a statistically significant factor in the outcome of a variety of diseases, conditions, and phenomena.

Methods

To investigate its relevance in the context of a stem cell transplant (SCT), we examined its influence in chronic myeloid leukaemia, a disease with well-established prognostic factors. Data were collected on 626 patients who received a first myeloablative allogeneic SCT between 1981 and 2006. Star sign was determined for each patient.

Results

Univariate analyses comparing all 12 individual star signs showed considerable variation of 5-year probabilities of survival, 63% for Arians, to 45% for Aquarians, but without significance (P .65). However, it was possible to pool together star signs likely to provide dichotomous results. Thus, grouping together Aries, Taurus, Gemini, Leo, Scorpio, and Capricorn (group A; n 317) versus others (group B; n 309) resulted in a highly significant difference (58% vs 48%; P .007). When adjusted for known prognostic factors in a multivariate analysis, group B was associated with an increased risk of mortality when compared with group A (relative risk [RR], 1.37; P .005).

Conclusion

In this study, we show that, providing adequate care is taken, a significant relationship between patient star sign and survival post SCT for CML can be observed. This is, however, a completely erroneous result, and is based on the pooling together of observations to artificially create a statistically significant result. Statistical analyses should thus be carried out on a priori hypotheses and not to find a meaningful or significant result.

http://www.transplantation-proceedings.org/article/S0041-1345(10)01081-X/fulltext

Commentary

Dr Dileepa Ediriweera,
Lecturer in Medical Informatics at Faculty of Medicine,
University of Kelaniya, Sri Lanka.

This study shows the how the data can be manipulated to obtain a statistical significance and the. Individual variable analysis (i.e. considering each zodiac sign as a categorical variable, hence a variable with 12 categories) showed no significant association between zodiac sign and 5-year survival probabilities. However, artificially categorizing them into two categories (Group A - Aries, Taurus, Gemini, Leo, Scorpio, and Capricorn vs rest considering as Group B) showed significant survival difference between the two groups. Further, the association remains significant even after adjusting for other prognostic factors where Group B showed poor survival probability. Therefore, authors highlight the importance of having a priory hypothesis before the statistical analysis and not to find meaningful or significant results during the analysis.

Anticoagulants (extended duration) for prevention of venous thromboembolism following total hip or knee replacement or hip fracture repair

Rachel Forster, Marlene Stewart

Cochrane Systematic Reviews
First published: 30 March 2016
Editorial Group: Cochrane Vascular Group
DOI: 10.1002/14651858.CD004179.pub2

(Adapted and quoted from Cochrane review Summary)

Background

It is common practice to administer prophylaxis using low-molecular-weight heparin (LMWH) or unfractionated heparin (UFH) until discharge from hospital, usually seven to 14 days after surgery. International guidelines recommend extending thromboprophylaxis for up to 35 days following major orthopaedic surgery but the recommendation is weak due to moderate quality evidence.

Objectives

To assess the effects of extended-duration anticoagulant thromboprophylaxis for the prevention of venous thromboembolism (VTE) in people undergoing elective hip or knee replacement surgery, or hip fracture repair.

Search methods

The Cochrane Vascular Information Specialist searched the Specialised Register (last searched May 2015) and CENTRAL (2015, Issue 4). Clinical trials databases were searched for on going or unpublished studies.

Selection criteria

"Randomised controlled trials assessing extended-duration thromboprophylaxis (five to seven weeks) using accepted

prophylactic doses of LMWH, UFH, vitamin K antagonists (VKA) or direct oral anticoagulants (DOAC) compared with short-duration thromboprophylaxis (seven to 14 days) followed by placebo, no treatment or similar extended-duration thromboprophylaxis with LMWH, UFH, VKA or DOACs in participants undergoing hip or knee replacement or hip fracture repair.

Data collection and analysis is done according to Cochrane guidelines."

Author's conclusion suggests:

"Moderate quality evidence suggests extended-duration anticoagulants to prevent VTE should be considered for people undergoing hip replacement surgery, although the benefit should be weighed against the increased risk of minor bleeding. Further studies are needed to better understand the association between VTE and extended-duration oral anticoagulants in relation to knee replacement and hip fracture repair, as well as outcomes such as distal and proximal DVT, reoperation, wound infection and healing."

Commentary

Hiran Amarasekera

Consultant Orthopaedic Surgeon, NFTH, Malabe

Hip Preservation Fellow.

University Hospitals of Coventry and Warwickshire, U.K.

Anticoagulant therapy following orthopaedic surgery mainly total hip and knee arthroplasty and hip fracture surgery has been a point of debate for many years all across the world. Even though there is some evidence that some form of anticoagulant therapy should be given post-operatively to prevent DVT, Whether this therapy prevents fatal PE (Pulmonary embolism) remains a question yet fully not answered.

Secondly the duration of anticoagulant therapy following above surgeries remains another point of debate. In UK most hospitals recommend therapy be given 10-14 days following knee replacement and 28-35 days following a hip replacement.

Thirdly the a detail risk assessment of bleeding VS DVT has not been addressed in these patients, and the risk of minor complications such as post operative bleeding, wound oozing, and infection caused by anticoagulant therapy.

A patient dying of PE as a complication of one of the above surgeries, not on anticoagulants is difficult to justify in a court of law,. However is there enough evidence to show increase in survival rates following anticoagulant therapy post-operatively?

A systematic review done by the Cochrane group (Vide Supra) tries to answer part of the question with regard to how long should We treat these patients.

After a major review authors still conclude that anticoagulants should be given with caution

Risk of bleeding should be carefully weighed against risk of DVT. According authors conclusions of above study We still need more studies to achieve clarity on duration of treatment and development of DVT.

While trying to answer these question with more studies the big questions still remain un answered.

- What is percentage of proximal DVT leading to PE?
- Does anticoagulants reduce the mortality following PE in this patient group?
- What is the contribution of anticoagulant therapy towards minor post-operative complications such as wound oozing, delayed healing, infection, post-operative bleeding etc.?

With all the debates studies and some evidence obtained in the past it appears that these questions will still need more research in coming years to get the full answers.

Association of Same Day Discharge With Hospital Readmission After Appendectomy in Pediatric Patients

Cairo S.B et al

JAMA Surg. 2017;152(12):1106-1112.

Importance

Appendectomy is the most common abdominal operation performed in paediatric patients in the United States. Studies in adults have suggested that same-day discharge (SDD) after appendectomy is safe and does not result in higher than expected hospital readmissions.

Objective

To evaluate the influence of SDD on 30-day readmission rates following appendectomy for acute appendicitis in paediatric patients.

Design, Setting and Participants

This retrospective cohort study used the American College of Surgeons National Surgical Quality Improvement Program–Paediatric database to evaluate 30-day readmission rates among paediatric patients who underwent an appendectomy for acute, non-perforated appendicitis. Patients selected for inclusion (n = 22 771) were between ages 0 and 17 years and underwent appendectomy for uncomplicated appendicitis between January 1, 2012, and December 31, 2015. Patients excluded were those discharged more than 2 days after surgery.

Exposures

Same-day discharge after appendectomy or discharge 1 or 2 days after surgery.

Main Outcomes and Measures

The primary outcome was 30-day readmission. Secondary outcomes included surgical-site infections and other wound complications.

Results

Of the 20 981 patients, 4662 (22.2%) had SDD and 16 319 (77.8%) were discharged within 1 or 2 days after surgery. The patient cohort included 12 860 boys (61.3%) and 8121 girls (38.7%), with a mean (SD) age of 11.0 (3.56) years. There was no difference in the odds of readmission for patients with SDD compared with those discharged within 2 days (adjusted odds ratio [aOR], 0.82; 95% CI, 0.51-1.04; P = .06; readmission rate, 1.89% vs 2.33%). There was no significant difference in reason for readmission on the basis of discharge timing. Likewise, there was no difference in wound complication rate between patients with SDD and those discharged 1 or 2 days after surgery (aOR 0.75; 95% CI, 0.56-1.01; P = .06).

Conclusions and Relevance

In paediatric patients with acute appendicitis undergoing appendectomy, SDD is not associated with an increase in 30-day hospital readmission rates or wound complications when compared with discharge 1 or 2 days after surgery. Same-day discharge may be an applicable quality metric for the provision of safe and efficient care for paediatric patients with acute, non-perforated appendicitis.

Commentary

Dr Dulantha de Silva

Senior Lecturer in Surgery

General Sir John Kotelawala Defence University, Sri Lanka

Appendectomy for uncomplicated appendicitis has long been considered as a potential candidate for day case surgery. This large database based cohort study seeks to buttress the argument in favour of day case appendectomy. The authors have looked at readmission and complication rates of patients discharged within two days of surgery in a paediatric population and found no adverse outcomes associated with same day discharge. These findings do hold relevance to our practice, especially given the social issues associated with prolonged hospital stays for children.

The negative predictive value of a negative repeat urinalysis in patients presenting with haematuria: A review of 1138 patients

Benjamin Zak Starmer, Amal Singh, Stephen Bromage.

J Clin Urol. 2017; 10 (5,): 471 – 475.

https://doi.org/10.1177/2051415817711633

Objective

Haematuria may be transient for a number of benign conditions, particularly a urinary-tract infection (UTI). We set out to determine if a negative repeat urinalysis at the time of urological assessment for patients with haematuria could predict negative investigations and whether investigations could be tailored by this test.

Methods

This was a retrospective analysis of records for all patients attending a haematuria clinic between 16 September 2013 and 12 September 2014. This included patients with visible and non-visible (microscopic) haematuria.

Results

There were 1138 patients, 599 with visible haematuria (VH) and 460 with non-visible haematuria (NVH). Seventy-two patients were excluded. A total of 546 patients had a positive repeat urinalysis for blood; 438 patients had a negative repeat urinalysis when tested at the haematuria clinic, 298/599 for VH and 140/460 NVH. For those who had negative repeat urinalysis, urothelial cancer was found in 15/298 VH and 1/140 NVH. The one patient with negative repeat urinalysis and NVH was found to have a grade 2 (high grade) bladder tumour. The negative predictive value for a negative repeat urinalysis in transient haematuria was 0.95 for VH and 0.99 for NVH. Twenty-nine patients with VH and repeat negative urinalysis on assessment had a positive urine culture suggesting a UTI as a cause. None of these patients was found to have urothelial cancer (p = 0.0413).

Conclusion

Patients who experience transient VH and subsequent repeat negative urinalysis in the absence of infection have a 5% chance of urothelial cancer and should still be investigated. For those with transient NVH, the probability of finding a urothelial cancer is <1%, although we did find a high-grade bladder tumour in this group. If patients have a positive urine culture and a negative repeat urinalysis following treatment, they could be spared haematuria investigations.

Commentary

Ajith Malalasekera
Consultant Urological Surgeon.
Senior Lecturer, Department of Anatomy,
Faculty of Medicine, University of Colombo, Sri Lanka

The above study reinforces the guidelines indicating the need to investigate those with visible haematuria to completion. The detection of a single high grade bladder cancer, though "statistically" a low number, among those with non visible haematuria patients cannot be discarded lightly. However, the recommendation of sparing those with a positive urine culture and a negative repeat urinalysis after treatment is pragmatic. Also utilizing the positive or negative status of a repeat urinalysis to prioritise patients for investigation can be useful in resource poor settings.

Panel of Reviewers 2017

The editorial board of the Sri Lanka Journal of Surgery would like to greatly thank the panel of reviewers for their time and invaluable assistance.

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