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Case Series

Minimally invasive surgery in women with endometrial cancer on haemodialysis: a tertiary centre experience

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ABSTRACT

The aim of the case series was to determine if minimally invasive approach to cancer staging is safe and feasible for patients on haemodialysis. We looked at patients on haemodialysis with endometrial cancer who underwent minimally invasive hysterectomy bilateral salpingo-oophorectomy with pelvic lymph node dissection performed by the Gynaecological Oncology unit at Singapore General Hospital from 2016 to 2020. Their demographics, operative details, oncological outcomes, and any post-operative complications were recorded. A total of 16 haemodialysis patients undergoing either laparoscopic or robotic endometrial cancer staging were selected. In our case series, mean duration of surgery was 173 minutes. Mean post-operative high dependency unit stay was 1 day with mean total length of hospitalisation of 5 days. All patients were ambulant at 24 hours post-surgery with pain scores peaking at 2 out of 10 at 6 hours post-surgery, and declining to 0 at 12 hours post-surgery. None of the patients experienced post-operative fluid dysfunction, electrolyte imbalance, sepsis, venous thromboembolism, cardiovascular or wound related complications. We conclude that minimally invasive surgical techniques is a safe and viable approach to endometrial cancer staging for patients on haemodialysis. Further refinement and streamlining of various strategies in the pre-, intra-, and post-operative period can further improve patient outcomes and quality of care.

Keywords: Pre-operative, Post-operative, Surgical complications, Safe alternative

INTRODUCTION

Surgical risks in patients on haemodialysis has been known to be higher than that in patients with minimal medical comorbidities. There is a 1-4% overall risk of surgical mortality, which rises to as high as 20% when applied to patients with concomitant diabetes mellitus and age above 60 years old. Patients with end-stage renal disease (ESRD) remain longer in intensive care units and are hospitalised for extended periods of time when compared to patients who do not have renal disease.[1,2] Most patients with ESRD also have other co-existing medical comorbidities such as ischaemic heart disease (IHD), hypertension (HTN) and diabetes (DM). These will further increase surgical morbidity and mortality rates. Currently there are few studies that investigate mortality and morbidity rates specifically for patients with end stage renal failure undergoing hysterectomy. In general surgery, the estimated morbidity rates in this group of patients range from 14-64%, with common causes of morbidity being difficulties in fluid volume regulation and electrolyte imbalances. Hyperkalaemia is the most common complication, followed by infection, bleeding and arrhythmias. Other noteworthy causes of morbidity include anaemia, neuropathy, and port site infections.[3] There have been multiple studies performed investigating the use of laparoscopy in endometrial cancer surgical staging. These trials did not mention the exclusion of ESRD patients. A 2012 Cochrane review showed a significantly lower rate of severe post-operative adverse

events in patients undergoing laparoscopic staging, with no significant difference in mortality or disease recurrence rates.[4] This was further validated in a 2018 Cochrane review which examined nine randomised controlled trials comparing laparoscopy with laparotomy surgical management, particularly in early-stage endometrial cancer. The authors concluded no difference in overall survival and disease-free interval with laparoscopic surgical staging in patients with presumed early-stage disease. Operative morbidity and hospital stay were reduced in the laparoscopy group.[5] As of the writing of this paper, there is no large-scale meta-analysis or review comparing the outcomes of specifically patients with ESRD on haemodialysis undergoing minimally invasive endometrial cancer staging. The reason for this might be due to the small population size of these patients or that minimally invasive cancer staging may not be routinely offered to this group of patients due to their medical comorbidities resulting in alternative treatment options being offered instead. Our analysis presents a novel opportunity to investigate this unique group of patients in an Asian context allowing us to reflect and learn from our experience to better optimise future management.

CASE SERIES

Patient demographics

Sixteen patients were recruited in our case series. Our patients were middle aged, with a mean age of 59 years. They were also overweight, with a mean BMI of 28.8. Racial distribution was evenly divided into the Chinese and Malay racial populations. Most of them had cardiovascular risk factors such as HTN, DM, and cardiovascular disease (which includes congestive heart failure and previous IHD). Thirteen out of sixteen patients had an ASA (American Society of Anaesthesiologist) score of 3. 25% of the patients had a history of abdominal surgeries and 53% have had previous major surgery not withstanding abdominal surgeries including one with endovascular aneurysm repair and one with thyroidectomy.

Pre-operative information

All the patients in this case series had stage 5 chronic kidney disease with a mean eGFR ranging from 3 to 15, therefore, they were on haemodialysis pre-operatively. All patients had mild anaemia with mean haemoglobin value of 10.6 g/dl. All patients were on antiplatelet and/or anticoagulants pre-operatively. Pre-operative staging was based on imaging with computed tomography and magnetic resonance imaging, which classified all patients in the early stage of either stage 1A or 1B.

Intra-operative information

All patients underwent minimally invasive approach surgery for endometrial cancer, with 68.8% having laparoscopic approach and the remaining 31.3% undergoing robotic endometrial cancer staging. Fifteen of the sixteen patients underwent pelvic lymphadenectomy with only one patient that underwent laparoscopic endometrial staging surgery for whom lymphadenectomy was not performed. The reason for the omission of pelvic lymphadenopathy was that this patient was deemed to have early-stage disease with pelvic lymph nodes that were not found to be enlarged after intra-operative assessment. The mean duration of surgery was 172.9 min.

Post-operative outcomes

None of the patients required intensive care unit monitoring and 81.3% required high dependency ward monitoring in the immediate post-operative period. However, stay in high dependency units was short and most were transferred to general ward on post-operative day one. The average length of hospitalization was 5.1 days with a wide range from 2 to 11 days. Median duration of total hospital stay was 5 days. 50% had a length of stay less than five days total. All patients complained of mild pain six hours post-surgery, which resolved completely after twelve hours. There were no complications of fluid volume dysfunction, electrolyte imbalance, sepsis, venous thromboembolism, cardiovascular complications, wound complications during inpatient stay.

Mean post-operatively haemoglobin value was 10.4 g/dl which was only slightly lower than that pre-operatively. 18.8% required blood transfusion post-surgery, however these patients already had low pre-operative haemoglobin count. Three patients had a history of IHD, and all had one unit of packed cells given on the day after surgery. The three patient's haemoglobin trend are as follows. Among the patients who underwent oncological surgical staging, most were in the early stages. Fifteen of the sixteen patients had stage 1A or 1B endometrial cancer. The remaining patient was diagnosed with stage 3C1 disease.

Five patients did not require any adjuvant treatment, nine required vault radiation therapy (RT) due to stage 1B or higher-grade histology (G2 or G3), one required small field RT and one required combined chemotherapy RT. Of the sixteen patients, one had passed away as of the date of writing of this paper due to brain metastases and one was lost to follow-up. The other fourteen patients were still alive and were being followed up in our gynae-oncology clinic. There were no mortalities as a consequence of surgery.

Table 1: Patient demographics.

Variables		Values
Age (years), mean (range)		59.3 (50-70)
Race	Malay	9

Continued.

Variables		Values
	Chinese	7
BMI (m/kg^2), mean (range)		28.8 (19.2-35.2)
Cardiovascular risk factors	Hypertension	15
	Diabetes	9
	Ischemic heart disease	8
History of previous surgery	Abdominal surgery only	4
	Lower segment caesarean section	2
	Laparoscopic radical nephrectomy	1
	Endovascular aneurysm repair	1
ASA score	2	2
	3	13
	4	1

Table 2: Patients who required blood transfusion.

Patient number	Pre-operative haemoglobin level	Haemoglobin level immediately post-operation	Haemo-globin level after 1 unit packed red cells trans-fusion
1	9.5	7.1	8.8
2	9.8	7.6	9
3	10.5	8.7	9.8

Table 3: Patient operative details.

Details		
Pre-operative		
Haemoglobin (g/dl), mean (range)		10.6 (9.5-12.1)
Mean eGFR, mean (range)		7 (3-15)
Mode of dialysis		All patients were on haemodialysis
Antiplatelet/anticoagulant		All patients were on antiplatelet
Pre-operative radiological staging	Stage 1A	13
	Stage 1B	3
Intra-operative analysis		
Surgical approach	Laparoscopy	11
	Robotic	5
Lymphadenectomy	Nil	1
	Pelvic lymphadenectomy	15
Duration of surgery (mins), mean (range)		172.9 (120-250)
Estimated blood loss (ml)		150.0 (100-300)
Complications		Nil intra-operative complications
Post-operative outcomes		
Post-operative monitoring (days), mean (range)	High dependency unit	0
	High dependency unit	01.1 (0-2)
Length of hospitalisation (days), mean (range)		5.1 (2-11)
Post-operative haemoglobin (g/dl), mean (range)		10.4 (9.3-11.7)
Pain score, mean (range)	6 h	2 (2-6)
	12 h	0.5 (0-2)
	24 h	0
Post-operative day of ambulation, mean (range)		1 (0-2)
Post-operative complications	Grade 1	0

Continued.

Details		
	Grade 2: anaemia requiring transfusion	3
	Grade 3	0
	Grade 4	0
	Grade 5	0
Adjuvant therapy	Nil	5
	Vault RT	9
	Small field RT	1
	Chemo RT	1
Final histology	Endometrioid	16
	Grade 1	6
	Grade 2	8
	Grade 3	2
Surgical staging	1A	10
	1B	5
	2	0
	3A	0
	3B	0
	3C1	1
	3C2	0
	4	0
Survival	Mortality at time of writing	1 (due to brain metastasis)
	Loss to follow up	1
	Currently on follow up	14

DISCUSSION

The primary aim of this case series is to investigate the operative details, post-operative, and oncological outcomes of patients with ESRD on haemodialysis undergoing minimally invasive surgical staging at our institution; and from there determine if minimally invasive approach is a safe and feasible option for this group of patients. The secondary aim is to develop a clinical pathway for these select patients at our centre.

SGH is a tertiary referral centre for patients with complex medical comorbidities. Such patients are referred here for review by the consultant gynae-oncologists after being diagnosed with gynaecological malignancies. Further investigations such as imaging might be scheduled to assess the pathology and guide further management and treatment.

All patients are discussed at the weekly multidisciplinary team (MDT) meeting, attended by the gynae-oncology surgeons, medical oncologists, radiation oncologists, radiologists, pathologists, and specialist nurses. Recommendation for management will be determined by this team. Patients are jointly managed in an MDT consisting of relevant medical specialists such as cardiovascular medicine, endocrine, renal and anaesthesia alongside allied healthcare professionals such as physiotherapist, dietitian, and nurse specialists.

Surgeries are performed within 4 to 8 weeks from time of diagnosis with delays usually due to additional time taken to optimise their medical conditions. Chronic medications are also reviewed and adjusted accordingly. For example, in our case series, all patients were on aspirin due to their history of IHD or other vascular pathologies. Clopidogrel was stopped for 5 days prior to surgery whereas aspirin was continued throughout. Pre-operative dialysis arrangements are also made to ensure the patients were well optimised up to the day of surgery.

Patients are scheduled for admission on the same day as surgery. The surgery is performed by a gynae-oncology surgeon with MIS experience who will decide on the use of different MIS surgical techniques- such as conventional laparoscopy, single port laparoscopy or robotic surgery.

Post-operatively, patients are transferred to surgical high dependency unit for closer monitoring and usually stepped down to general ward the following day. Patients are encouraged to resume oral feeds and ambulate as soon as possible. Routine analgesia such as paracetamol and oral opioids are given to alleviate post-operative pain. Intravenous antibiotics are continued for 1 day post-operatively and then continued via oral intake for 1 week after. While this practise is not in line with international surgical antibiotic prophylaxis guidelines, due to the immune-compromised state of ESRD patients we modified our practice to extend course of antibiotics usage. The renal team would assist in the care of the patient,

reviewing their fluid status and arranging their post-operative dialysis schedule. Patients are advised to continue heparin free dialysis for at least one-month post-surgery.

Upon discharge, patients will be followed up in the outpatient clinic. The gynae-oncology specialist nurse is actively involved in the post-operative care and any observations would be reported to the surgical team. Histological results from the surgery would be discussed at the MDT meeting and appropriate adjuvant treatment would be recommended. Patients would then be followed up once every 4 months to assess for recurrence.

2 flowcharts summarising the patient journey from referral to post-operative care are provided below.

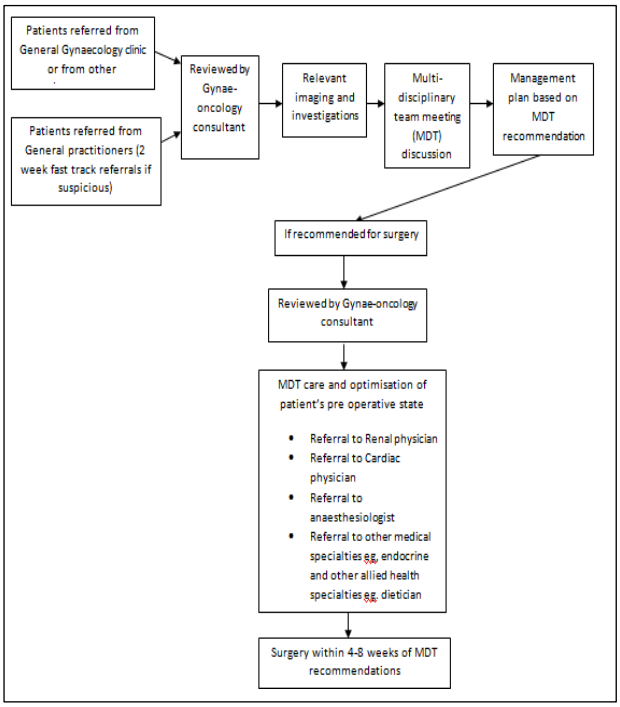

Figure 1: Patient pre-operative experience.

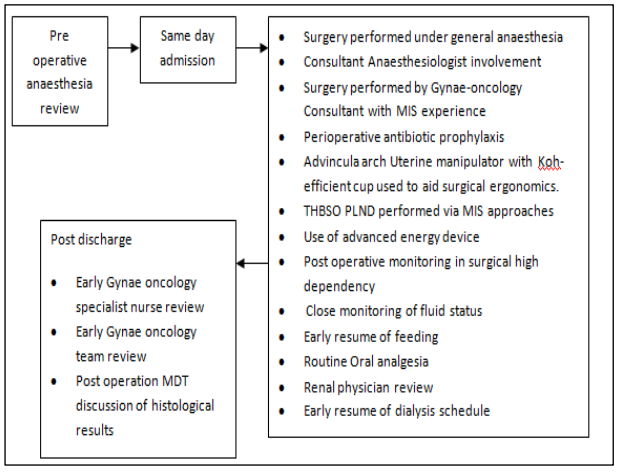

Figure 2: Patient inpatient operative journey.

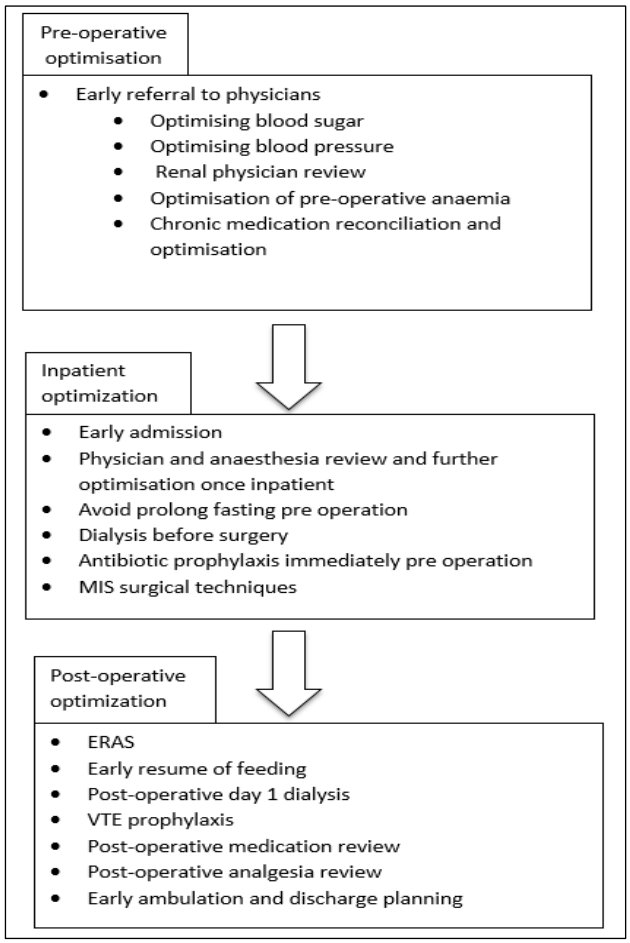

Figure 3: Overview of the care of ESRD patients on haemodialysis undergoing MIS endometrial cancer staging surgery.

Recommendations

HTN and DM are common among ESRD patients. A pre-operative review of blood pressure and glycaemic control is essential to ensure optimal titration of their medications. Anti-hypertensives should not routinely be stopped and oral medication that cannot be served post-operatively should have its route of administration revised. Optimisation of blood glucose pre- and post-operatively can help reduce diabetes related complications such as infections and hyperglycaemic crisis. Patient's fluid status and weight should also be monitored closely both before and after surgery and taken into consideration for any fluid prescriptions.

Myocardial dysfunction and other cardiovascular events were among the greatest cause of mortality in patients with ESRD. An up-to-date cardiac risk assessment via stress testing, rhythm assessment, and risk factor screening with a view to cardiac revascularization pre-operatively may help reduce intra-operative cardiac risk and enhance operative survival.[6] Vascular access may also be challenging in this group of patients. Therefore, early communication with anaesthetists in charge can allow early review and arrangements put in place to help secure

venous access. ESRD patients are likely to develop anaemia due to reduced erythropoietin production. Correcting pre-operative anaemia may help alleviate the adverse effects of operative blood loss. While there is currently no definite recommendation on safe pre-operative haematocrit levels, a study by Brenowitz et al. showed an increase in intra-operative complications in ESRD patients with haematocrit ranging from 20 to 26 %.[7] Full blood count and iron stores should be checked prior to surgery, and administration of intravenous ferritin or erythropoietin taken into consideration under the guidance of the renal physician.

Uraemia is known to interfere with platelet function by impairing platelet aggregation and adhesiveness, usually due to glycoprotein dysfunction.[8-11] Uraemic plasma contents are also known to impair platelet function, and intensification or initiation of dialysis is often recommended for severely uraemic patients who are bleeding or awaiting invasive procedures.[12] Use of heparin free dialysis the day before or day of the surgery can not only help reduce this uraemia induced platelet dysfunction but also achieve euvolemia and normal electrolyte levels.[13] Heparin used during haemodialysis has a residual anticoagulant effect and can last up to 2 hours after. This effect on intra- and post-operative bleeding is uncertain; therefore, heparin-free dialysis is recommended in the 12 hours prior to surgery.[2] Due to the increased intra-operative blood loss, we recommend use of heparin free dialysis up to 1-month post-surgery.

Enhanced recovery after surgery (ERAS) are evidence-based programs that have been shown to improve post-operative outcomes for patients undergoing major surgery. Introducing ERAS principles into care of these patients where possible can improve their post-operative clinical outcomes. In our experience, good practices such as early refeeding and antimicrobial prophylaxis led to improved outcomes and reduced complications.

Our experience has shown that MIS techniques for endometrial cancer staging in ESRD patients to be comparable to the general population of patients undergoing similar surgery. Data from the 2018 Cochrane review of 9 randomised controlled trials involving general population of patients undergoing laparoscopic staging showed that mortality rate was 6-17% over the follow up period of median duration ranging between 38.5 months to 7 years. Peri-operative mortality within six weeks post-surgery was 0.63%. Rate of visceral injuries include bladder at 1.09%, ureteric at 0.82% and bowel at 2.18%, and rate of vascular injury was 2.49%. Blood transfusion was required in 6.20% of patients. Length of hospitalisation was between an average of 2.1 to 8.6 days[5]. In our case series, there were no mortality and intra-operative complications. Hospitalisation was also comparable with a range of 2 to 11 days. The main reason behind delay in discharge was the additional time needed for the patient and her caregivers to coordinate post-discharge care. One way to reduce this delay would be to begin discharge planning pre-operatively by early engagement of medical social welfare teams. Blood transfusion rate in our patients however was higher at 18.8%. This was attributed to increased intra-operative blood loss which was more likely in ESRD patients due to uraemia and use of anti-platelet therapy. We have since changed our practice and stopped anti-platelet agents up to 1-week pre-surgery when possible.

CONCLUSION

This case series demonstrated that post-operative complications in this challenging group of patients were comparable to rates quoted in reviews for general population of patients undergoing laparoscopic staging. This has shown that MIS is a safe and viable approach to endometrial cancer staging surgery in patients with renal failure in tertiary institutions with multi-disciplinary support. Care for patients on haemodialysis undergoing endometrial cancer staging can be streamlined with careful management of their medical co-morbidity and early identification of issues that might complicate their hospital stay. With better planning and monitoring protocols, we can even consider day surgery or short hospitalisations for well-optimised patients on haemodialysis in the future.

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