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Original Article

Postoperative acute renal failure in patients with gynecologic malignancies: analysis of 10 cases and review of the literature

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Objective: Postoperative acute renal failure (PO-ARF) is an important cause of mortality among surgical patients. Although there have been many reports on PO-ARF after cardiac surgery and liver transplantation, less is known about the risk of PO-ARF after gynecologic operations. We aimed to investigate the risk of PO-ARF on gynecologic malignancy operations.
Methods: 1,155 patients' medical charts were reviewed who underwent therapeutic surgery for gynecologic malignancies from January 1, 2005 to December 31, 2007, at the Asan Medical Center, Seoul, Korea.
Results: Of these, 10 patients, comprising 0.89% of those who underwent radical hysterectomies and 0.86% of those who underwent debulking operations, were diagnosed with PO-ARF. Their mean age was 61.9±10.1 years. Five patients had preoperative risk factors. Mean operating time was 360.8±96.2 minutes. Five patients experienced intra-operative hypotension and all patients were given blood transfusions during surgery. Eight patients underwent hemodialysis, with two continuing on dialysis to date. Only two patients fully recovered.
Conclusion: Patients undergoing surgery for gynecologic malignancies may be at high risk for PO-ARF, because of old age, long operation times, and profuse bleeding. It is necessary to monitor these patients for postoperative renal function and urine output. If a postoperative oliguric state is detected, aggressive volume expansion should be started immediately, followed by hemodialysis.

Key Words: Postoperative acute renal failure, Gynecologic malignancy

INTRODUCTION

Postoperative acute renal failure (PO-ARF) is a major cause of mortality in surgical patients. The incidence of PO-ARF varies from 1.1% to 17%, depending on the type of surgery,[1,2] and is especially high in patients who undergo major vascular, cardiac, and high-risk abdominal surgeries, including Coronary Artery Bypass Graft, aortic surgery, and surgery for obstructive jaundice.

Generally, gynecologic surgery is not associated with a high risk of PO-ARF. However, operations for gynecologic malignancies, such as radical hysterectomies and debulking operations, may cause PO-ARF. Although there have been many reports describing PO-ARF after cardiac surgery and after liver and kidney transplantations, less is known about PO-ARF after gynecologic surgery.

We therefore describe 10 patients with gynecologic malignancies, who experienced PO-ARF at our institute over a three-year period.

MATERIALS AND METHODS

We retrospectively reviewed the medical records of the 1,155 patients who underwent elective radical surgery for gynecologic malignancies at the department of gynecologic oncology of Asan medical center, Seoul, Korea, between January 1, 2005, and December 31, 2007, to identify all patients who experienced PO-ARF. Of these, 10 patients were diagnosed with PO-ARF. We reviewed these 10 patient's medical records including operation-records, laboratory data, and follow-sheets of nephrology. We interviewed the patients who referred to local clinic by telephone to know current state of their original malignancy and renal problem.

PO-ARF is defined as a sudden sustained decline in glomerular filtration rate (GFR) associated with azotemia and a fall

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in urine output after operation. In this study, it was diagnosed by a nephrologist after determination of postoperative anuria or abnormal increases in blood urea nitrogen and creatinine.

Patients with preoperative abnormal renal function and those who died of multi-organ failure within few days after surgery were excluded.

RESULTS

1. Patient characteristics (Table 1)

Over the 3 year study period, 10 patients were diagnosed with PO-ARF. Their mean age was 61.9±10.1 years, and this was 13 years greater than the mean age (about 49 years) of the 1,155 patients who underwent surgery for gynecologic malignancies during the same time period. Five of the 10 patients had preoperative risk factors. Four had hypertension, which was being treated with medication, with one of these (patient 2) also having diabetes mellitus and liver cirrhosis, and one patient (patient 7) had a history of angina and cerebrovascular accident.

2. Types of surgery (Table 2)

ARF developed in 4 of the 445 patients (0.89%) who underwent open or laparoscopic radical hysterectomies and pelvic lymph node dissections with paraaortic lymph node sampling for cervical cancer; in 5 of the 435 patients (1.15%) who underwent debulking operations, including total abdominal hysterectomy, bilateral salpingo-oophorectomy, pelvic and paraaortic lymph node dissection, and total or partial omentectomy with or without other mass excision, for ovarian cancer or primary peritoneal carcinomatosis, in 1 of the 260 patients who underwent operations for endometrial cancer (0.38%).

All operations were performed by gynecologic oncologists with more than 5 years of experience.

3. Drugs and anesthetics (Table 3)

All patients received a third-generation cephalosporin as a prophylactic antibiotic and non-steroidal anti-inflammatory drugs (NSAIDs) as painkillers. Two patients (patients 1 and 4) received aminoglycoside injections before the development of ARF. Seven of the 10 patients were anesthetized with sevo-

Table 1. Patient characteristics

Case	Age	Patient history	Diagnosis	Op name	Adjuvant Tx.	Last status, F/U (month)
1	69	-	Ovarian cancer IIIc	TAH, BSO, PLND, PALND, T-O, inc-app.	CTx.	NED, 18
2	74	HTN, DM, HBV LC	Ovarian cancer Ia	TAH, BSO, PLND, PALND, T-O, inc-app.	-	NED, 14
3	76	HTN	Peritoneal carcinomatosis	TAH, BSO, PLND, PALND, T-O, inc-app.	-	PD, 17
4	74	HTN, epilepsy	Endometrial cancer IIIc	TAH, BSO, PLND, PALND, T-O, inc-app.	CTx.	Expired
5	55	HTN	Cervical cancer Ib1	RH, BSO, PLND, PALNS, inc-app.	-	NED, 15
6	47	-	Cervical cancer Ib1	LRH, PLND, PALNS	-	NED, 15
7	59	Angina, CVA	Ovarian cancer IVb	TAH, BSO, PLND, PALND, T-O, LAR, ileo-cecal R&A	CTx.	PR, 16
8	57	-	Cervical cancer Ib1	RH, BSO, PLND, PALNS, inc-app.	-	NED, 15
9	54	-	Cervical cancer Ib2	RH, BSO, PLND, PALNS, inc-app.	RTx.	NED, 12
10	51	-	Ovarian cancer IIIc	TAH, BSO, PLND, PALND, T-O, inc-app. LAR, spleen mass exc.	CTx.	PR, 11

TAH: total abdominal hysterectomy, BSO: bilateral salpingo-oophorectomy, PLND: pelvic lymph node dissection, PALND: paraaortic lymph node dissection, T-O: total omentectomy, inc-app: incidental appendectomy, PALNS: paraaortic lymph node sampling, LAR: low anterior resection, R&A: resection and anastomosis, exc: excision, CTx: chemotherapy, RTx: radiotherapy, F/U: follow-up, NED: no evidence of disease, PD: progression of disease, PR: partial response, HTN: hypertension, DM: diabetes, CVA: cerebrovascular accident

Table 2. Types of surgery and morbidities of postoperative ARF cases

	Cervical cancer		Ovarian cancer* & peritoneal carcinoma†		Endometrial cancer		Other cancer	Total
	Laparotomy	Laparoscopy	Debulking op.	Laparoscopic staging op.	Laparotomy	Laparoscopy		
Total	220	225	420	15	128	132	15	1,155
ARF	3	1	5	0	1	0	0	10
Morbidity	1.36	0.4	1.9	0	0.78	0	0	0.87
(%)	0.89		1.15		0.38			

ARF: acute renal failure, op: operation
*,† same operative procedures

flurane and the other 3 with isoflurane.

4. Development of intra-operative hypotension, transfusions, and operation times (Table 4)

Intra-operative hypotension, under 90/60 mm Hg, developed in five patients. All 10 patients were given blood transfusions during surgery, with three of them patients receiving more than 5 but less than 10 packs of Packed Red Blood Cells (PRBCs).

Mean operating time was 360.8±96.2 minutes. Eight operations took more than 300 minutes, with only two (patient 3 and 4) requiring less than 300 minutes of surgery.

5. Postoperative laboratory findings

Urinalysis within the first 24 hours after operation showed that four patients were positive for occult blood and three for micro-albuminuria. The mean change in pre-to-post-operative hemoglobin concentration was -0.92 g/dL, with three patients having postoperative hemoglobin levels below 10 g/dL. Four patients had postoperative platelet counts below 100,000/mm^3 (69,000-91,000/mm^3). Two patients showed slight increases in activated partial thromboplastin time (aPTT) levels (to over 50 seconds) (Table 4). Early (within 24 hours) postoperative blood urea nitrogen/creatinine (BUN/Cr) levels were within normal ranges in all 10 patients, but became elevated within 1 or 2 days. At the time of ARF diagnosis, BUN concentration was over 60 mg/dL in two patients and Cr concentration was over 4.5 mg/dL in five patients (Table 5).

6. Types of renal failure and durations of hemodialysis

Anuric type ARF (urine output < 50 mL/day) was observed in six patients, oliguric type ARF (urine output < 400 mL/day) in three, and non-oliguric type ARF in one (patient 2) (Table 5).

ARF was diagnosed by nephrologists about 3.5±0.9 days after surgery. Immediate hemodialysis was started in eight patients, two of whom remain on hemodialysis to date. Of the remaining six patients, one (patient 4) died 3 months later because of progression of endometrial cancer, and the other five underwent hemodialysis for a median of 40 days (range, 14 to 66 days).

7. Clinical outcomes

At a median time from ARF diagnosis of 14.7 months (range,

Table 3. Drugs and anesthetics used, and durations of anesthesia

Case	aminoglucosides	NSAID	Furosemide	Anesthesia time (min)	Anesthetics
1	O	O	O	365	Sevoflurane
2	-	-	O	305	Isoflurane
3	-	O	O	347	Sevoflurane
4	O	O	O	270	Sevoflurane
5	-	O	O	390	Isoflurane
6	-	O	O	420	Sevoflurane
7	-	O	O	480	Isoflurane
8	-	O	O	350	Sevoflurane
9	-	O	O	415	Sevoflurane
10	-	O	O	310	Sevoflurane

NSAID: non-steroidal anti-inflammatory drug, O: used

Table 4. Operating times, transfusion amounts, and postoperative hematologic findings

Case	Operating time (min)	Intraop. hypotension* (mmHg)	Intraop. transfusion (pack)	Postop. (<24 hr) Hb (mg/dL)	Postop. platelet ($\times 10^3/mm^3$)	Postop. aPTT (sec)	Postop. UA
1	337	-	P(8), F(8)	10.5	131	41.8	Alb (TR)
2	237	82/46	P(3)	10.7	80	46.1	OB (+)
3	311	-	P(3)	11.8	70	45.6	NS
4	254	74/50	P(6)	11.9	107	39.1	RBC (m), Alb (+)
5	355	-	P(4)	12.9	69	43.6	glc (+)
6	384	-	P(3)	11.8	91	-	NS
7	431	78/40	P(7), F(4)	9.6	246	52.4	NS
8	332	86/54	P(4)	11.4	138	38.0	OB (+)
9	391	-	P(4)	9.3	124	-	OB (+), Alb (+)
10	576	88/46	P(3), F(2)	9.3	198	55.9	OB (+)

aPTT: activated partial thromboplastin time, -: absent or not checked, P: PRBC, F: FFP, Postop: within 24 hours after operation, UA: urine analysis, Alb: albumin, TR: trace, +: positive, OB: occult blood, NS: non-specific, m: many i.e., RBC(m), gross hematuria, glc: glucose
*lowest level of BP

Table 5. Hemodialysis and individual clinical courses of ARF patients

Case	Dx. of ARF (POD)	Dur. of HD (day)	BUN/Cr (mg/dL)			FENa: Dx. of ARF	Cause of ARF	Clinical feature of ARF	F/U
			Postop (<24 hr)	Dx. of ARF	Last F/U				
1	4	43	18/0.7	58/5.8	20/1.5	11.4	ATN	Anuric	P-R
2	2	-	16/1.4	24/2.5	31/2.0	1.5	ATN	Non-oliguric	P-R
3	2	+	21/1.1	36/3.9	44/7.4	12.2	ATN	Anuric	CRF
4*	5		30/1.1	36/3.9		-	ATN	Anuric	Expired
5	4	23	30/1.0	66/6.2	8/0.7	21.9	ATN	Oliguric	F-R
6	3	14	21/1.1	36/3.9	13/0.8	16.7	ATN	Oliguric	F-R
7	4	-	11/0.6	35/2.2	21/1.8	0.24	Hypo-volemia	Oliguric	P-R
8	4	40	19/0.9	60/5.9	38/1.9	4.3	ATN	Anuric	P-R
9	4	+	15/0.5	51/6.7	91/12.6	34.1	ATN	Anuric	CRF
10	3	66	19/1.0	40/5.2	41/3.6	2.4	ATN	Anuric	P-R

ARF: acute renal failure, BUN/Cr: blood urea nitrogen/creatinine, FENa: fractional excretion of sodium, Dx: time diagnosis, Dur: duration, POD: postoperative date, HD: hemodialysis, -: not performed or not checked, +: still continuing, F/U: follow up, P-R: partial recovery, F-R: full recovery, CRF: chronic renal failure

*died because of cancer progression 4 months after operation

11 to 18 months), only two patients (patients 5 and 6) have fully recovered, with normal ranges of BUN/Cr and GFR. Two patients (patients 3 and 9) were diagnosed with chronic renal failure (CRF), with creatinine levels over 4.5 mg/dL, and have been treated continuously with hemodialysis. One patient died because of progression of her original malignancy. The remaining five patients have partially recovered from PO-ARF, in that they have no symptoms of renal failure without dialysis, but their levels of BUN/Cr and GFR remain abnormal.

Seven of 10 patients have been followed without evidence of disease. Three of these received adjuvant therapy after primary curative surgery. One patient died from progression of original disease and another two patients are receiving conservative therapy (Table 1).

DISCUSSION

Depending on the definition of the condition and the nature of the surgery, the incidence of PO-ARF varies from 1.1-17%.[1,2] The mortality rate from ARF following cardiac surgery, even with dialysis, has been reported to be as high as 63%.[3] We found that the incidence of PO-ARF was 0.87% in patients undergoing surgery for gynecologic malignancies over 3 year-period. We could not estimate mortality rate, because no patient died of ARF alone.

Postoperative mild renal dysfunction can be treated by early management of renal hypovolemia, but prolonged renal hypovolemia may induce renal parenchymal damage such as renal tubular necrosis.[4] It means early diagnosis and early management are more important than continuous treatment. Among 10 cases, only 2 patients fully recovered and another 2 patients progressed to CRF, despite continuous hemodialysis. But, unfortunately in this study, we could not find any significant differences at time interval for diagnosis or hemodialysis in fully recovered two cases.

One of the important preoperative risk factor for PO-ARF is old age,[5] especially over 50 combined with underlying diseases such as hypertension or diabetes mellitus.[6] The mean age of our 10 patients was 61.9±10.1 years, and 5 had underlying diseases known to be risk factors for ARF. As this study, many gynecologic cancer patients who underwent surgical treatment are often older than 50 and have many other risk factors.

Several drugs commonly used in the preoperative or postoperative periods are known to be nephrotoxic.[7] All 10 patients were treated with more than one nephrotoxic drug, including prophylactic antibiotics and NSAIDs. Two patients (1 and 4) were initially treated with aminoglycosides, but these drugs were stopped immediately after development of oliguria. Compared with other 8 cases, these drugs would not contribute to the severity or rapidity of ARF, as indicated by levels of BUN/Cr, time to ARF development, duration of hemodialysis, and follow-up levels of BUN/Cr.

Generally, anesthetics reduce urine output, GFR, renal blood flow, and excretion of electrolytes. Acute alteration of renal function has been reported after use of sevoflurane,[8] but other authors have reported no changes in renal function.[9,10] We observed no significant differences in the courses of ARF in patients anesthetized with sevoflurane, compared with isoflurane.

Preoperative and postoperative intravascular blood volume has a great impact on development of PO-ARF, and massive intra-operative bleeding or hypotension frequently cause PO-ARF.[5] As this study, many patients who underwent gynecologic malignancy operation experienced intra-operative hypotension and were given massive blood transfusions.

Except these general risk factors, gynecologic malignancy operations have several special risk factors for PO-ARF. Which are urinary tract injury and increased intra-abdominal

pressure (IAP). Increased IAP may reduce GFR and cause anuria.[11] IAP can develop frequently during laparoscopic operations adapted to treat various gynecologic malignancies. To date, laparoscopic radical hysterectomy for cervical cancer and laparoscopic staging operation for endometrial cancer are often performed for early stages. In this study, we found that only 1 of 372 patients (0.27%) who underwent laparoscopic surgery developed PO-ARF. For considering of IAP as risk factor of PO-ARF, further studies are needed. Although there was no obstructive renal failure in this study, many gynecologic operations may cause obstructive renal failure arising from intra-operative ureteral injury.

Even though, many surgeons have hesitated about the management of aggressive volume expansion because of the risk of pulmonary edema, volume expansion alone may be sufficient to prevent ARF.[12] It has been reported that aggressive volume expansion could reduce the need for dialysis and could decrease mortality rates from 70% to 28% in postoperative patients.[13] Furosemide is a loop diuretic that decreases the metabolic demand of renal tubular cells, reducing their oxygen requirements and thereby increasing their resistance to ischemia.[14] All 10 patients received furosemide at commencement of oliguria or elevated BUN/Cr levels. In some patients, urine output increased slightly, but the progress of ARF was not halted. Although our results can not provide convincing evidence for use of furosemide as a prophylactic agent against PO-ARF, furosemide may allow free fluid manipulation.[15]

Although some authors reported that early frequent hemodialysis does not reduce the incidence of sepsis and mortality in post-traumatic ARF patients,[16] hemodialysis may improve prognosis. Thus, most of our patients were commenced on hemodialysis immediately after diagnosis of ARF.

In conclusion, it is very difficult to recover renal function after development of postoperative ARF. Patients undergoing surgery for gynecologic malignancies have many risk factors for PO-ARF, old age, long operation times, profuse bleeding, and some risks of ureteral injuries. It is therefore necessary to monitor these patients with postoperative renal function and urine output. If a postoperative oliguric state is detected, aggressive volume expansion should be started immediately, with or without furosemide, followed by hemodialysis.

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