

Acute Normovolemic Hemodilution for Radical Retropubic Prostatectomy and Radical Cystectomy

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OBJECTIVES	Radical retropubic prostatectomy (RRP) and radical cystectomy (RCx) are well tolerated and widely performed. Because intraoperative blood loss is one of the most common problems, we performed acute normovolemic hemodilution (ANH) to prevent allogenic blood transfusion (ABT). In this study we tried to clarify the safety, effectiveness and problems of ANH at urologic operations.
METHODS	The study included 169 patients who underwent RRP and 97 patients underwent RCx from April 2003 to March 2006. The eligible patients for ANH were required to have preoperative hemoglobin of 12 g/dL or more without history of myocardial ischemia. The amount of blood collected was 800 mL in RRP and 800 mL or 1200 mL in RCx. Neoadjuvant chemotherapy was performed in 11 (11.3%) of 97 patients with RCx.
RESULTS	ANH was available in 164 (97.0%) of 169 patients in RRP and 41 (42.3%) of 97 patients in RCx. All 11 (11.3%) patients who received neoadjuvant chemotherapy before RCx revealed anemia and all were excluded from ANH. No patients had an hypovolemic event develop during the autologous blood being stored. The median volume of intraoperative blood loss was 1400 mL in 164 RRP and 19 patients (11.6%) required ABT. In 41 patients undergoing RCx, the median volume of blood loss was 1720 mL and 13 patients (32.5%) required ABT. In the postoperative period, no patients had cardiovascular or pulmonary complications develop originated from ANH.
CONCLUSIONS	ANH is a safe and useful method of transfusion during RRP and RCx. ANH can be recommended for patients who need these operations. UROLOGY 72: 401–405, 2008. © 2008 Elsevier Inc.

Radical retropubic prostatectomy (RRP) and radical cystectomy (RCx) are standard treatments for prostate and bladder cancers, respectively. These operations are well tolerated by patients and widely performed by urologists in clinical practice.

However, a significant volume of blood loss sometimes occurs in these operations. To compensate blood loss, autologous blood transfusion is preferable to allogenic transfusion to avoid risks for infection by unidentified virus and immunosuppression.

Preoperative autologous blood donation (PAD) is the safest blood replacement as assessed by the American Medical Association Counsel of Scientific Affairs.¹ However, it is one of flaws of PAD that the number of units donated

preoperatively usually far exceeds the number actually used. Multicenter studies indicated that approximately 50% of autologous blood units collected were discarded and not transfused.^{2,3} In addition, PAD is inconvenient, time-consuming, and time limited. It is also expensive because recombinant human erythropoietin is sometimes used. Thus, recent studies also demonstrated that PAD is not cost-effective and of questionable benefit.⁴

Acute normovolemic hemodilution (ANH) is a removal of whole blood with a simultaneous volume replacement with either crystalloid or colloid solution at the time of surgery. The removed blood is transfused at the end of surgery for compensating blood loss. Hemodiluted patients with a lower hematocrit in surgery lose a smaller volume of red blood cells than those with higher hematocrit. Some studies have already indicated that ANH has many advantages in several surgical procedures.^{5–7} In urologic surgery, the usefulness of ANH has been reported in RRP.^{4,8–12} However, there are few reports on the other urologic surgery.¹³ In this context, we

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Submitted: July 6, 2007, accepted (with revisions): November 2, 2007

Table 1. Clinical characteristics of patients who received acute normovolemic hemodilution

	Patients with RRP (164)	Patients with RCx (41)
	Median (range)	Median (range)
Age (yr)	67 (44–77)	65 (35–79)
Body weight (kg)	65.7 (47.0–87.0)	60.5 (43.0–85.0)
BMI (kg/m ²)	24.3 (18.4–32.3)	23.5 (16.3–29.2)
Preoperative Hb (g/dL)	14.3 (11.9–18.2)	13.8 (11.4–17.6)
Collected blood volume (mL)	800 (360–1200)	1200 (600–1200)
Operative time (min)	220 (145–345)	460 (340–645)
Intraoperative blood loss (mL)	1400 (210–5300)	1720 (600–4550)
ASA score	1:61 2:102 3:1	1:15 2:26 3:0
Urinary diversion	—	Ileal conduit: 33 Ileal neobladder: 7 Ureterostomy: 1

RRP, radical retropubic prostatectomy; RCx, Radical cystectomy; BMI, body mass index; Hb, hemoglobin; ASA score, American Society of Anesthesiologists Score; Ureterostomy, cutaneous ureterostomy.

examined the usefulness of ANH for patients with RCx as well as those with RRP.

PATIENTS AND METHODS

The subjects were 169 patients who underwent RRP for localized prostate cancer, and 97 patients who underwent RCx for bladder cancer or urethral cancer at our hospital from April 2003 to March 2006. The eligible patients for ANH were required to have 12 g/dL or higher level of preoperative hemoglobin (Hb). Those who had the history of myocardial ischemia were excluded from the study. After endotracheal intubation, hemodilution process was started. Blood drawn was simultaneously replaced with an equal volume of 6% hydroxyethyl starch. If hemodynamic status was not stable, acetated Ringer's solution was added. The amount of blood collected was 800 mL for RRP and 800 mL or 1200 mL for RCx, but the final amount was decided by an anesthesiologist in charge, depending on clinical profiles and conditions of patients. We did not use the target hematocrit or the formula to calculate blood volume to be removed. No patients received administration of the recombinant human erythropoietin. All patients provided written informed consent on ANH before surgery.

The anesthesiologist decided when the autologous blood was returned to patients, depending on intraoperative Hb, hemodynamic status, and an amount of blood loss. The collected blood was returned basically to all patients irrespective of patients' conditions during the surgery. If patient's hemodynamic status was not stable after autologous blood was returned, allogenic blood was transfused, which was clinically judged by anesthesiologists.

RRP with the limited pelvic lymph node dissection was performed by 20 urologists, including residents in training under the supervision of a senior surgeon according to the standard method.¹⁴ RCx with pelvic lymph node dissection extending to the level of the aortic bifurcation was also performed by 15 urologists according to the standard method.¹⁵ In regard to urinary diversion, an ileal conduit, Studer's ileal neobladder, or cutaneous ureterostomy was constructed according to extension and pathologic features of the disease, performance status and patients' preference.

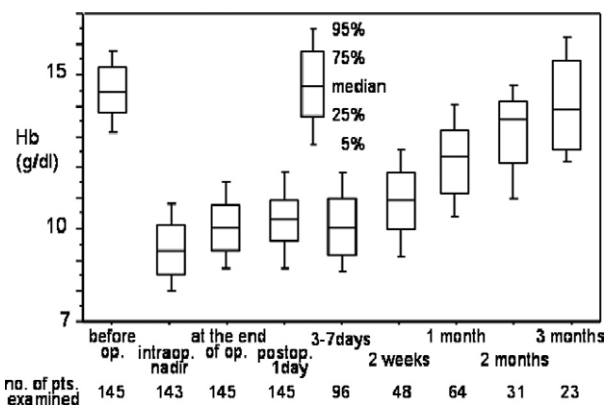


Figure 1. The changes of hemoglobin for the patients with RRP who received acute normovolemic hemodilution with no additional allogenic blood transfusion.

Blood cell count was determined routinely 2 weeks before, during, and at the end of operation, followed by that on the first postoperative day. The count was additionally determined if necessary. Neoadjuvant chemotherapy before surgery was given for 11 (11.3%) of 97 patients with bladder cancer or urethral cancer. A combination of methotrexate, vinblastine, doxorubicin, and cisplatin (M-VAC) was used for a total of 10 patients, including 2 cycles for 7, 1 for 2, and 3 for 1. Another patient received 2 cycles of fluorouracil plus cisplatin before operation. The study did not include patients who received adjuvant chemotherapy after surgery. Operation time, amount of blood loss, and laboratory data were reviewed from medical charts.

Background factors of patients and their clinical outcomes were analyzed with Mann-Whitney's *U* test with statistical significance considered to be $P < 0.05$.

RESULTS

A total of 169 patients undergoing RRP and 41 patients undergoing RCx were included in this study. ANH was available in 164 (97.0%) of 169 patients and 41 (42.3%)

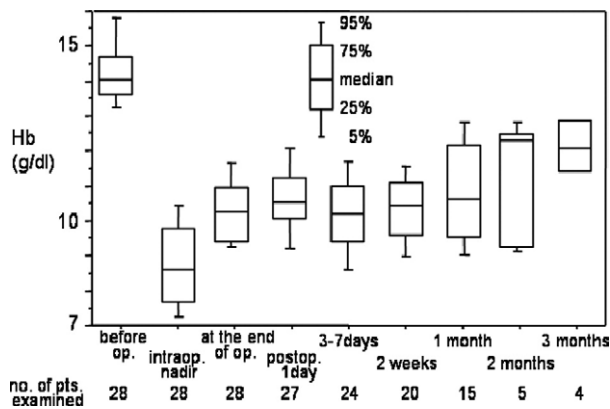


Figure 2. The changes of hemoglobin for the patients with RCx who received acute normovolemic hemodilution with no additional allogenic blood transfusion.

of 97 patients. In patients with RRP, 3 were excluded from ANH because of anemia, and 2 because of ischemic heart disease (IHD). In patients with RCx, 50 patients were excluded because of anemia, 5 because of IHD, and 1 because of poor general condition. All 11 patients who received neoadjuvant chemotherapy before RCx had anemia preoperatively, which did not allow them to receive ANH.

The clinical characteristics of patients who received ANH were shown in Table 1. No patients had hypovolemic state develop, such as hypotension or arrhythmia during storage of the autologous blood. In RRP, the median volume of intraoperative blood loss was 1400 mL and 19 patients (11.6%) required allogenic blood transfusion. In RCx, the volume was 1720 mL and allogenic transfusion was needed for 13 patients (32.5%).

Figures 1 and 2 show the changes of Hb in patients with RRP and RCx who did not use allogenic blood transfusion. Although not all patients were thoroughly evaluated after return of their Hb after operation, patient with RRP Hb tended to return within 2 months after surgery. In contrast, the return was seemingly delayed after 3 months postsurgery in patients with RCx.

We compared clinical features of patients who did not require allogenic blood transfusion (ANH group) and those who did require the additional allogenic blood transfusion (ABT group) (Tables 2 and 3). In patients undergone RRP, concentration of Hb before surgery, intraoperative amount of blood loss, operative time, and hospitalization period were significantly different between the 2 groups. In the patients who had undergone RCx, body weight, the concentration of Hb before surgery, and intraoperative blood loss were significantly different between the groups.

In the postoperative period, no patients had cardiovascular or pulmonary complications develop that originated from ANH.

COMMENT

ANH was first introduced by Messmer in 1975 as a means of lowering red cell mass in operation.¹⁶ At the start of surgery, patients have whole blood removed with a simultaneous volume replacement. During surgery, hemodiluted patients lose a smaller volume of red cells. And at the end of surgery, removed autologous blood is returned to patients. ANH have many advantages, including those that can be easily obtained in the operating room, there is no need for a place to preserve it, there is no fear of infection, and the blood collected contains many coagulation factors.

In this study, 97.0% of patients with RRP were able to be managed with ANH. The rate of additional transfusion by using allogenic blood was 12.5%. In previous studies, the rates were reported from 8.2% to 20%,^{4,8,9,11-13} suggesting that the current result was comparable to previous ones. The results in RCx group raise clinical issues to be discussed. First, ANH was available only in 42.3% of all patients treated with RCx. Second, the rate of additional transfusion of allogenic blood was 32.5%, which was higher than it of RRP, although we consider that ANH is still effective for avoiding allogenic transfusion in patients with RCx.

Several factors may be involved in the lower rate of conducting ANH in patients with RCx. These factors are myelosuppression caused by neoadjuvant chemotherapy, preoperative anemia caused by continuous macrohematuria, and poor performance status of elderly patients in the current study. The efficacy of neoadjuvant chemotherapy has already been reported in the treatment of muscle-invasive bladder cancer.¹⁷ However, as was found in the current study, neoadjuvant chemotherapy-induced myelosuppression may not allow us to use ANH in some patients. Adjuvant but not neoadjuvant may be beneficial for some patients with muscle-invasive bladder cancer who need chemotherapy in the adjuvant setting. Thus, the issue remains to be determined.

There may be a bias in evaluating perioperative and postoperative changes of Hb because it was periodically not measured in all patients. However, the current results may safely indicate that decreased Hb in patients with RRP returns within 2 months after surgery and that in those with RCx, within 3 months. Thus, the regular measurement of Hb is not necessary for the patients who are treated with ANH unless otherwise indicated.

CONCLUSIONS

ANH was safely performed for patients with RRP and RCx. It contributed to avoiding allogenic blood transfusion. However, in some patients with RCx, neoadjuvant chemotherapy caused preoperative anemia that made ANH difficult to be provided.

Table 2. Clinical features of patients with radical retropubic prostatectomy who received acute normovolemic hemodilution alone or required additional allogenic blood transfusion

	ANH Group: 145 Patients	ABT Group: 19 Patients	P-Value
	Median (range)	Median (range)	
Age (yr)	67 (44–77)	68 (57–75)	0.85
Body weight (kg)	65.9 (47.1–84.0)	65.4 (47.0–87.0)	0.70
BMI (kg/m ²)	24.4 (18.4–30.1)	23.7 (20.1–32.3)	0.91
Preoperative Hb (g/dL)	14.4 (11.9–18.2)	13.5 (11.9–15.9)	0.01
Collected blood volume (mL)	800 (360–1200)	800 (600–820)	0.87
Operative time (min)	220 (145–345)	250 (180–300)	0.01
Intraoperative blood loss (mL)	1350 (210–3500)	2800 (850–5300)	<0.0001
ASA score (No. of patients)	1:54 2:90 3:1	1:7 2:12 3:0	0.99
Hospitalization period (d)	15 (10–41)	17 (12–25)	0.03

ANH, acute normovolemic hemodilution; ABT, allogenic blood transfusion; BMI, body mass index; Hb, hemoglobin; ASA score, American Society of Anesthesiologists Score.

ANH group consisted of patients who received acute normovolemic hemodilution but did not require additional allogenic blood transfusion.

ABT group consisted of those who needed additional allogenic blood transfusion.

Table 3. Clinical features of patients with radical cystectomy who received acute normovolemic hemodilution alone or required additional allogenic blood transfusion

	ANH Group 28 Patients	ABT Group 13 Patients	P-Value
	Median (range)	Median (range)	
Age (yr)	63.5 (44–79)	72 (35–77)	0.71
Body weight (kg)	61.5 (43.5–85.0)	56.0 (43.0–79.1)	0.04
BMI (kg/m ²)	23.7 (19.2–29.2)	22.8 (16.3–27.3)	0.28
Preoperative Hb (g/dL)	14.1 (12.6–17.6)	13.6 (11.4–15.7)	0.02
Collected blood volume (mL)	1200 (600–1200)	800 (600–1200)	0.08
Operative time (min)	447.5 (340–580)	480 (405–645)	0.24
Intraoperative blood loss (mL)	1435 (600–2900)	2650 (1400–4550)	0.0004
ASA score (no. of patients)	1:10 2:18	1:5 2:8	0.88
Hospitalization period (d)	30 (20–108)	36 (15–62)	0.62
Urinary diversion	Ileal conduit: 22 Ileal neobladder: 5 Ureterostomy: 1	Ileal conduit: 11 Ileal neobladder: 2 Ureterostomy: 0	0.63

ANH, acute normovolemic hemodilution; ABT, allogenic blood transfusion; BMI, body mass index; Hb, hemoglobin; ASA score, American Society of Anesthesiologists Score.

ANH group consisted of patients who received acute normovolemic hemodilution but did not require additional allogenic blood transfusion.

ABT group consisted of those who needed additional allogenic blood transfusion.

The reduced Hb returned to normal within a few months after surgery without any management. Thus, the regular measurement may not be needed, unless otherwise indicated.

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