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Intraoperative red blood cell salvage and autologous transfusion during open radical retropubic prostatectomy: a cost–benefit analysis

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ABSTRACT

INTRODUCTION Open radical retropubic prostatectomy (RRP) has an average blood loss of over 1,000ml. This has been reported even from high volume centres of excellence.[1–4] We have looked at the clinical and financial benefits of using intraoperative cell salvage (ICS) as a method of reducing the autologous blood transfusion requirements for our RRP patients.

MATERIALS AND METHODS Group A comprised 25 consecutive patients who underwent RRP immediately prior to the acquisition of a cell saver machine. Group B consisted of the next 25 consecutive patients undergoing surgery using the Dideco Electa (Sorin Group, Italy) cell saver machine. Blood transfusion costs for both groups were calculated and compared.

RESULTS The mean postoperative haemoglobin was similar in both groups (11.1gm/dl in Group A and 11.4gm/dl in Group B). All Group B patients received autologous blood (average 506ml, range: 103–1,023ml). In addition, 5 patients (20%) in Group B received a group total of 16 units (average 0.6 units) of homologous blood. For Group A the total cost of transfusing the 69 units of homologous blood was estimated as £9,315, based on a per blood unit cost of £135. This cost did not include consumables or nursing costs.

CONCLUSIONS We found no evidence that autologous transfusions increased the risk of early biochemical relapse or of disease dissemination. ICS reduced our dependence on donated homologous blood.

KEYWORDS

Blood transfusion – Cell saver – Intraoperative cell salvage – Open radical retropubic prostatectomy – Prostate specific antigen

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Open radical retropubic prostatectomy (RRP) has long been considered a gold standard surgical treatment for localised prostate cancer. The treatment of choice is now moving in favour of the minimally invasive alternatives such as laparoscopic and robotically assisted radical prostatectomy. Open surgery has been associated with considerable blood loss. Average blood loss of over 1,000ml has been reported even from high volume centres of excellence.[1-4] As a consequence, donated homologous blood transfusion (HBT) is frequently required. This is associated with significant risks, including allergic reactions and the transmission of blood borne infections.[5] Concern has also been raised about the immunologic effect of homologous transfusions as well as the risk of cancer recurrence.[6]

Various methods such as preoperative blood donation, preoperative erythropoietin injections, acute normovolaemic haemodilution (ANH) and intraoperative cell salvage (ICS) are used to compensate for blood loss and to avoid the need for allogenic blood transfusion (ABT). Despite the fact that autologous blood abolishes the risk of alloimmunisation, transfusion reactions and the transmission of infections, it has not found universal favour for clinical and practical reasons. The drawbacks and benefits of these different modalities have been the subject of much discussion. Although ICS has been shown to significantly reduce the amount of ABT reactions, the risk of disseminating cancer cells has been a theoretical concern.[7] Studies have, however, demonstrated that ICS does not adversely affect the long term outcomes of patients undergoing uro-oncologic surgery. There is no evidence to support the concern about the theoretical risk of cancer dissemination.[7–9] We have looked at the clinical and financial benefits of using ICS as a method of reducing the ABT requirements for our RRP patients.

TABLE 1 The comparative values of haemoglobin, haematocrit and transfusion rate in Group A and B

		Group A	Group B	*p* value
Haemoglobin (gm/dl and range)	Preoperative	14.8 (11.3–16.9)	15.4 (12.8–18.4)	0.410
	2nd Post-operative day	11.1 (9.2–12.5)	11.4 (9.2–13.5)	0.188
Homologous blood transfused (units and mean)		69 (2.8)	16 (0.6)	
Surgeon 1	Number of patients	14	11	
	Blood units transfused	32	10	
Surgeon 2	Number of patients	11	14	
	Blood units transfused	37	6	

Patients and Methods

The study involved 50 consecutive patients undergoing open RRP for localised prostate cancer. Patients were divided into two groups. Group A comprised 25 consecutive patients who underwent RRP immediately prior to the acquisition of a cell saver machine; Group B consisted of the next 25 consecutive patients undergoing surgery using the cell saver machine. All procedures were performed by one of two surgeons (SV and GS) using a similar open RRP technique in both groups.

Patients in Group A received HBTs when indicated. Requirement was assessed based on perioperative haemoglobin, intraoperative blood loss and clinical vital sign assessments including heart rate and blood pressure measurements. Intraoperatively, the decision to transfuse homologous blood was taken considering a combination of factors that included the amount of intraoperative blood loss, anticipated future blood loss, haemodynamic parameters and intraoperative spot haemoglobin level measurements using a HemoCue® optical haemoglobinometer. In the postoperative period, haemoglobin levels were assessed from routine laboratory assay measurements.

Patients in Group B had their intraoperative blood loss suction recovered and processed through a Dideco Electa (Sorin Group, Italy) red blood cell salvage machine. Saline washing and centrifugation was used in the standard processing of the recovered blood. Processed blood was deposited in blood storage bags for subsequent transfusion. The processed, packed red cells were transfused back to the patient using an in-line LeukoGuard® RS leukocyte filter (Pall Corporation, Port Washington, US). All patients in Group B received their own salvaged processed blood, irrespective of the volume of blood lost or processed. In addition, they also received homologous blood if required, based on the same clinical parameters as for transfusion in Group A.

A postoperative haemoglobin of less than 9gm/dl was the threshold for HBT in both groups.

Preoperative and second postoperative day haemoglobin values were recorded for both groups. Cross-matched and HBT rates were also assessed. Prostate specific antigen (PSA) levels were measured 6 weeks postoperatively and at the routine 3-month follow up. Biochemical evidence of relapse, secondary procedures and the need for hormone therapy were compared between the two groups. Statistical analysis was performed using the Pearson's chi-square test. Blood transfusion costs for both groups were calculated and compared.

Results

The mean age of patients in Group A was 62.5 years (range: 48–73 years) and for Group B it was 59.2 years (range: 47–68 years) (p= 0.055). The mean postoperative haemoglobin was similar in both groups (11.1gm/dl in Group A and 11.4gm/dl in Group B). The mean preoperative and postoperative haemoglobin of both groups is detailed in Table 1.

For 6 patients in Group A, the decision to give homologous blood was taken intraoperatively. 10 patients in Group A had transfusions in the intraoperative and immediate postoperative period on day 0. One patient had homologous blood transfused on postoperative days 1 and 2. The main indication for these transfusions was intraoperative blood loss, which was significant enough to cause haemodynamic compromise.

In Group B, the 5 patients who received additional homologous blood were transfused on postoperative days 1 and 2 due to significant intraoperative loss and a postoperative haemoglobin drop to <9gm/dl.

There was an inter-operator difference noted in the rate of transfusions in both of the groups but it was not statistically significant (Table 1).

In Group A, 18 (72%) patients received a total of 69 units of homologous blood (average 2.8 units) in the perioperative period. The majority of the blood transfusions were intraoperative based on the assessment of the haemodynamic parameters. HBTs only on the first and second postoperative days were included in the data. All Group B patients received autologous blood (average 506ml, range: 103–1,023ml). In addition, 5 (20%) patients in Group B received a group total of 16 units (average 0.6 units) of homologous blood.

For Group A, the total cost of transfusing the 69 units of homologous blood was estimated as £9,315, based on a per blood unit cost of £135. This cost did not include consumables or nursing costs. For Group B, the cell salvage machine consumables, leukocyte filters, irrigation fluid and anticoagulants costs amounted to £77 per case. The total cost for Group B, including the 16 units of homologous blood used, was £4,085. The £4,200 purchase cost of the cell saver machine was recovered after just 20 cases.

The average length of hospital stay for Group A was 7 days (range: 4–17) and for Group B it was 5 days (range: 4–13) (p=0.0091). There were early biochemical relapses in both groups. PSA relapse was defined as a PSA of ≥0.2ng/ml on postoperative testing. The PSA results, Gleason score, staging and follow up of patients in both the groups are summarised in Table 2.

Discussion

Quoted blood loss for open RRP, even from high volume centres, has ranged from 300ml to 7,700ml and transfusion rates from 3.4% to 89%.[1–4,10,11] A better understanding of the pelvic anatomy and improved surgical technique has more recently lead to a significant decline in blood loss as low as 260ml and HBT requirements.[2,5,12] Nevertheless, in many centres blood loss is still significant and often requires intervention in the form of HBT. This has lead to the search for more effective alternatives to HBT. Options include transfusion of pre-deposited autologous blood donation (PAB), ANH and ICS. However, each has its benefits and drawbacks.

Pre-deposited autologous blood donation

PAB became a popular alternative to allogenic transfusion after the American Medical Association Council on Scientific Affairs considered it be safe.[13] However, not only is it time consuming and time constrained, it is also inconvenient for the patient. More importantly, studies have shown that it is associated with a blood discard rate of 31.5%, particularly since PAB blood can only be stored for a maximum of 5 weeks.[14] The use of PAB also fails to completely avoid the need for ABT. PAB is reported to be associated with ischaemic events and a higher risk of adverse reactions requiring hospitalisation.[15] It is also linked to the risk of bacterial contamination from skin commensals at the time of collection. As with all stored blood products, PAB must undergo microbiology investigations.[15] A significant number of patients undergoing RRP avoided HBT by either autologous blood transfusion and/or haemodilution and it was concluded that PAB is a financially more efficient autologous blood management option.[16,17]

Acute normovolaemic haemodilution

ANH has been used with considerable success to reduce HBTs. It has been shown to be cost effective. Since the blood transfused is autologous, the documented risk of

TABLE 2 Gleason scores, staging and follow up in Group A and B

	Group A	Group B
Gleason scores (postoperative)		
Gleason <7	5 (20%)	0 (0%)
Gleason ≥7	20 (80%)	25 (100%)
Pathological staging		
T2	20 (80%)	20 (80%)
T3	5 (20%)	5 (20%)
Postoperative PSA		
≤0.1	21 (84%)	24 (96%)
≤0.1	21 (84%)	1 (4%)
Follow up duration in months (range)	51 (24–80)	23 (1–35)
PSA relapse on subsequent follow up (≥0.2ng/ml)		
No	21 (84%)	24 (96%)
Yes	4 (16%)	1 (4%)

homologous blood-borne infections is eliminated. Clinically, patients tolerate ANH quite well; however, Monk *et al* demonstrated that the decrease in the arterial blood pressure was due to the anaemia produced by haemodilution.[18,19] Published blood transfusion guidelines recommend that, although extreme haemodilution is more efficacious, it should be restricted to relatively healthy patients with a low risk of ischaemic heart disease.[20] ANH has been shown in these studies to be a safe and effective method of blood conservation.

Intraoperative cell salvage

ICS has been shown to be clinically effective in replacing circulating volume and in maintaining tissue oxygenation by Gray *et al*.[9] The estimated blood loss was not significantly different between groups; however, homologous transfusion requirements were significantly less in the ICS group. ICS use also resulted in a higher postoperative haematocrit.

Although red cell salvage has been in routine use for non-cancer based surgery for quite some time, concerns regarding the theoretical risk of cancer dissemination have limited its use during cancer surgery. A number of authors have looked at this specific safety issue. It has been reported that cell saver use did not increase the risk of haematogenous metastases and also did not adversely affect the 5-year survival or prognosis of patients who underwent uro-oncological surgery.[21,22]

Studies have looked into the possible relationship between the use of cell saver and biochemical relapse of prostate cancer following RRP. Three separate studies conducted by Nieder *et al*,[7] Gray *et al*[9] and Davis *et al*[25] have assessed the difference in the biochemical recurrence rate in patients who had RRP with and without the use of cell saver. Biochemical relapses were noted in all three studies but the relapse rates within the groups were not significantly different. The 3-year disease-specific survival rate reported by Nieder *et al* was 72.2% and 73.0% in the ICS and non-ICS group respectively.[7] Gray *et al* found no difference in the incidence of progression-free survival with the use of ICS (p=0.41).[9] Davies *et al* reported that patients receiving ICS blood were less likely to develop a recurrence than those receiving autologous blood (odds ratio 0.81; 95% CI 0.33–2.00) or group 3 (odds ratio 0.66; 95% CI 0.21–2.08).[25]

Stoffel *et al* used a reverse transcription polymerase chain reaction assay for PSA mRNA to detect prostate cells in the cell-savaged and peripheral blood samples of patients during and following radical prostatectomy.[24] Although PSA expressing cells were found in the ICS blood of the majority of patients, they could not detect it in the peripheral circulation of any patients 3–5 weeks postoperatively with no biochemical failures.

Leukocyte depletion filters are routinely used for the re-transfusion of the processed autologous blood and markedly reduce the risk of re-instilling viable tumour cells from ICS salvaged blood in patients undergoing uro-oncologic surgery.[25,26]

There are a number of limitations in our study. Apart from a small cohort of non-randomised patients, our HBT rates for patients in the Group A were comparatively high. We believe that this was due to our practice of transfusing at the higher haemoglobin threshold of 9g/dL rather than the recommended UK level of 7g/dL.[27] ICS did, however, significantly reduce perioperative HBTs.

The unexpected finding of a shorter hospital stay in Group B was probably attributable to the fact that circulating volume and haemoglobin levels were better maintained at near optimal levels throughout the perioperative period, while for patients in Group A homologous transfusions were given more slowly on a catch-up basis throughout surgery and as required over postoperative days 1 to 2. The capital payback time for the purchase of a cell salvage machine is 20 cases, making it a very cost effective tool for radical prostatectomy blood loss replacement.

Conclusions

The use of ICS during RPP resulted in a significant decrease in the need for HBT. We found no evidence that autologous transfusions increased the risk of early biochemical relapse or of disease dissemination. ICS reduced our dependence on donated homologous blood. The cost benefits of ICS make this technique economically efficient, clinically effective and an attractive alternative to other methods of transfusion for open radical prostatectomy surgery.

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References

1. Stav K, Rahimi-Levene N, Lindner A *et al*. Retropubic radical prostatectomy: associated blood loss and transfusion requirements – a two decade perspective review. *Isr Med Assoc J* 2005; **7**: 103–106.
2. Nuttal GA, Cragun MD, Hill DL *et al*. Radical retropubic prostatectomy and blood transfusion. *Mayo Clin Proc* 2002; **77**: 1,301–1,305.
3. Barré C, Pocholle P, Chauveau P. Minimal blood loss in patients undergoing radical retropubic prostatectomy. *World J Surg* 2002; **26**: 1,094–1,098.
4. Rainwater LM, Segura JW. Technical consideration in radical retropubic prostatectomy: blood loss after ligation of dorsal venous complex. *J Urol* 1990; **143**: 1,163–1,165.
5. Goodnough LT, Brecher ME, Kanter MH, AuBuchon JP. Transfusion medicine. First of two parts – blood transfusion. *N Engl J Med* 1999; **340**: 438–447.
6. Bordin JO, Heddle NM, Blajchman MA. Biologic effects of leukocytes present in transfused cellular blood products. *Blood* 1994; **84**: 1,703–1,721.
7. Nieder AM, Carmack AJ, Sved PD *et al*. Intraoperative cell salvage during radical prostatectomy is not associated with greater biochemical recurrence rate. *Urology* 2005; **65**: 730–734.
8. Nieder AM, Manoharan M, Yang Y, Soloway MS. Intraoperative cell salvage during radical cystectomy does not affect long-term survival. *Urology* 2007; **69**: 881–884.
9. Gray CL, Amling CL, Polston GR *et al*. Intraoperative cell salvage in radical retropubic prostatectomy. *Urology* 2001; **58**: 740–745.
10. Paul R, Schmid R, Busch R *et al*. Influence of blood transfusions during radical retropubic prostatectomy on disease outcome. *Urology* 2006; **67**: 137–141.
11. Kordan Y, Barocas DA, Altamar HO *et al*. Comparison of transfusion requirements between open and robotic-assisted laparoscopic radical prostatectomy. *BJU Int* 2010; **106**: 1,036–1,040.
12. Walsh PC. Anatomic radical prostatectomy: evolution of the surgical technique. *J Urol* 1998; **160**: 2,418–2,424.
13. Council on Scientific Affairs. Autologous blood transfusion. *JAMA* 1986; **256**: 2,378–2,380.

14. Kajikawa T, Owari Y, Maeda K *et al*. The use of predeposited autologous blood transfusion for radical prostatectomy. *Nippon Hinyokika Gakkai Zasshi* 2002; **93**: 7–13.
15. Goodnough LT. Autologous blood donation. *Crit Care* 2004; **8 Suppl 2**: S49–52.
16. Noldus J, Gonnermann D, Huland H. Autologous blood transfusion in radical prostatectomy: results in 263 patients. *Eur Urol* 1995; **27**: 213–217.
17. Gilbert JB, Malkowicz SB, Wein AJ. Cell saver and radical retropubic prostatectomy: analysis of cost-effectiveness. *Urology* 1995; **46**: 542–544.
18. Monk TG, Goodnough LT, Birkmeyer JD *et al*. Acute normovolemic hemodilution is a cost-effective alternative to preoperative autologous blood donation by patients undergoing radical retropubic prostatectomy. *Transfusion* 1995; **35**: 559–565.
19. Monk TG, Goodnough LT, Brecher ME *et al*. Acute normovolemic haemodilution can replace preoperative autologous blood donation as a standard of care for autologous blood procurement in radical prostatectomy. *Anaesth Analg* 1997; **85**: 953–958.
20. British Committee for Standards in Haematology Blood Transfusion Task Force. Guidelines for autologous transfusion. II. Perioperative haemodilution and cell salvage. *Br J Anaesth* 1997; **78**: 768–771.
21. Vagner EA, Davidov MI. Blood reinfusion during nephrectomy in patients with kidney neoplasm. *Khirurgiia (Mosk)* 1998; **7**: 23–27.
22. Klimberg I, Sirois R, Wajsman Z, Baker J. Intraoperative autotransfusion in urologic oncology. *Arch Surg* 1986; **121**: 1,326–1,329.
23. Davis M, Sofer M, Gomez-Marin O *et al*. The use of cell salvage during radical retropubic prostatectomy: does it influence cancer recurrence? *BJU Int* 2003; **91**: 474–476.
24. Stoffel JT, Topjian L, Libertino JA. Analysis of peripheral blood for prostate cells after autologous transfusion given during radical prostatectomy. *BJU Int* 2005; **96**: 313–315.
25. Edelman MJ, Potter P, Mahaffey KG *et al*. The potential for reintroduction of tumour cells during intraoperative blood salvage: reduction of risk with use of the RC-400 leukocyte depletion filter. *Urology* 1996; **47**: 179–181.
26. Catling S, Williams S, Freites O *et al*. Use of a leucocyte filter to remove tumour cells from intra-operative cell salvage blood. *Anaesthesia* 2008; **63**: 1,332–1,338.
27. Murphy MF, Wallington TB, Kelsey P *et al*. Guidelines for the clinical use of red cell transfusions. *Br J Haematol* 2001; **113**: 24–31.