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Original Article

The impact of intra-operative cell salvage during open nephrectomy

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KEYWORDS
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Cost

Abstract *Objective:* To assess the impact of intra-operative cell salvage on outcomes in open nephrectomy.
Methods: A retrospective cohort study was performed of all patients undergoing open nephrectomy for suspected malignancy from 1 October 2013 to 1 October 2017. Patients were grouped and compared based on whether they received intra-operative cell salvage (ICS). Primary outcomes were allogeneic transfusion rates (ATRs), and if histology confirmed cancer, disease recurrence. Secondary outcomes were complications and transfusion-related cost.
Results: Forty patients underwent open nephrectomy for suspected malignancy during the enrolment period. Sixteen patients received ICS while 24 did not (standard group). Compared with the standard group, ICS patients had similar median age (63.5 *vs.* 61.0 years; $p = 0.83$) but fewer females (19% *vs.* 58%; $p = 0.013$). The groups were similar in pre-operative and discharge haemoglobin, Charlson Comorbidity Index, length of hospital stay and proportion with thoracoabdominal surgical approach. The ICS group had a smaller proportion undergoing partial nephrectomy (19% *vs.* 54%; $p = 0.025$) and shorter median follow-up (278 *vs.* 827 days; $p = 0.0005$). Histology was malignant for 14 ICS and 15 standard patients. The ICS group had more frequent ≥T2 disease (79% *vs.* 27%; $p = 0.005$). There were no positive margins. Both groups had similar ATRs (6% *vs.* 4%; $p = 0.96$), complication rates (19% *vs.* 29%; $p = 0.46$) and recurrence rates (18% *vs.* 7%; $p = 0.40$). Transfusion costs were higher amongst ICS patients (AUD $878.18 *vs.* $49.65 per patient).
Conclusion: ICS appears safe, with low rates of recurrence and complication. Both groups had low ATRs, and therefore cost benefit for ICS was not seen.

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1. Introduction

Renal cancer is the second most prevalent urological malignancy, with 338 000 new diagnoses worldwide in 2012 [1] and worsening cancer-specific mortality [2]. Nephrectomy is the most common treatment, and intra-operative haemorrhage remains a challenge. Even in high volume tertiary centres, allogeneic transfusion rates (ATRs) of 5%—30% [3—6] and 18%—45% [3,5,7] are reported for open partial and radical nephrectomy, respectively.

The development of well run blood banks have made allogeneic transfusion frequent in Western nations, with 14 million and 1.8 million units of red blood cells (RBCs) transfused annually in the USA and UK, respectively [8,9]. However, allogeneic transfusion has key issues of morbidity, cost, supply and poorer oncological outcomes. Transfusion-related acute lung injury, transfusion reactions, fluid overload and clerical error are familiar complications, contributing to an overall adverse event risk of 77 per 100 000 transfusions and death in 1 per 100 000 [8]. While rare at less than 1 per 1 million transfused RBC units, documented transfusion-transmitted infections (TTIs), bacterial and viral, still occur annually [8—10]. Blood is a perishable resource dependent on constant donations, and supply shortages are well known [11]. Transfusion is also expensive, with the administration of a single RBC unit costing approximately US Dollars (USD) $1000 in Australia and the USA and USD $600 in Western Europe [12,13]. Furthermore, a meta-analysis of patients undergoing nephrectomy has associated allogeneic transfusion with higher cancer specific mortality [14]. The mechanisms involved are unclear, but may involve transfusion mediated immunomodulation [15].

These concerns have encouraged methods to decrease ATRs. Fortunately, the modern urologist has a range of blood conservation techniques at their disposal. These include pre-operative supplementation with iron or erythropoietin, pre-operative autologous donation (PAD), acute normovolaemic haemodilution (ANH), restrictive transfusion thresholds and intra-operative cell salvage (ICS) [16,17]. However, each method holds challenges. Pre-operative supplementation is only applicable for patients with iron deficiency or anaemia, requires multiple healthcare episodes for testing, administration and re-testing, and may not be cost effective [16]. PAD became popular before effective screening existed for TTIs, particularly human immunodeficiency virus. However, PAD is expensive, discards approximately 50% of donated units and is now rarely used [16,18]. ANH involves intra-operative venesection, replacement with crystalloid or colloid, allowing the haemorrhage of dilute blood, then reinfusion of the patient's blood post-operatively. Despite being cost-effective, ANH may make patients hypocoagulable and is also not suitable for patients with pre-existing low haematocrit or cardiorespiratory comorbidities [16,19,20]. Restrictive transfusion practices are widely used and have clear benefit [21], but are not appropriate for patients with significant or symptomatic bleeding.

ICS involves the reinfusion of spilled blood. A dual-lumen sucker aspirates blood lost on the surgical field, adds heparinized saline or citrate via the second lumen to prevent coagulation, and stores this in a reservoir. When required, this fluid is washed and centrifuged to obtain a concentrate with haematocrit approximately 60%, passed through a leucocyte depletion filter to remove nucleated cells including bacteria and tumour cells, and reinfused [22]. The practice of ICS avoids many of the concerns of allogeneic transfusion. It virtually eliminates TTIs, more cost effective and supply is proportional to demand [8,16]. It is safe, with large audits of 18 000—64 000 units of reinfused ICS blood reporting complication rates of $<0.027\%$ [23—25]. Safety and efficacy have been proven in other specialties, with a Cochrane Review of 75 randomised controlled trials in cardiac, vascular or orthopaedic surgery finding ICS reduced ATRs by 38% [17]. However, urology has been slow to embrace ICS, due to concerns of equivocal benefit and reinfusion of malignant cells [26,27]. These fears have not been born out, with reassuring findings in a slew of uro-oncological studies including a meta-analysis [28—38].

To date, the only comparative study of ICS use in nephrectomy is Lyon et al.'s analysis [38] of patients undergoing open partial nephrectomy. This study aims to compare the outcomes of patients who did and did not receive ICS while undergoing open nephrectomy at our institution.

2. Materials and methods

A retrospective cohort study was performed, enrolling all patients undergoing open nephrectomy for suspected renal malignancy at our institution from 1 October 2013 to 1 October 2017 inclusive. Data were collected from hospital electronic and hard copy records. Patients were included regardless of whether partial or radical nephrectomy was performed, or whether laparotomy or thoracoabdominal surgical approach was utilised. Thoracoabdominal approach was defined as any supra-costal access. Patients were excluded if nephrectomy was performed for suspected urothelial malignancy, or for benign conditions, such as trauma or xanthogranulomatous pyelonephritis. All patients underwent surveillance for tumour recurrence, according to the Canadian Urological Association post-Nephrectomy Guidelines [39]. This represented at minimum assessment with history, examination, serum testing and chest X-ray examination annually, and computed tomography of the abdomen and pelvis at 2- and 5-year post-operatively. Disease recurrence included any local recurrence or distant metastasis.

Patients who did (ICS group) and did not (standard group) receive ICS were compared. Primary outcomes were ATRs, and disease recurrence among those with histologically confirmed cancer. Secondary outcomes were complications and transfusion-related cost. Complications were categorised based on the Clavien-Dindo grading system [40]. Ethics approval was granted by the Central Adelaide Local Health Network Human Research Ethics Committee, reference HREC/17/TQEH/255.

2.1. ICS practice

Our institution commenced using ICS for open nephrectomy in August 2015. Usage was intermittent, reserved for cases

deemed high bleeding risk, until in December 2016 it was decided to employ ICS routinely, allowing for surgeon preference, due to departmental review of evidence. We use the Fresenius Kabi CATSmart Continuous Autotransfusion System™, with a Haemonectics™ RS1VAE leucocyte depletion filter (LDF). As recommended by several authors [41,42], we use ICS in a financially tiered system. For all cases utilizing ICS, anticoagulated salvaged blood is collected in a reservoir (basic setup). When desired, this blood is then processed and reinfused (reinfusion setup). Thus, the ICS processor set and other single-use items are not wasted during cases where blood is not returned to the patient.

The transfusion trigger is decided by the anaesthetist, based on patient pre-operative haemoglobin, cardiorespiratory comorbidities, volume of blood collected, ongoing haemorrhage, intra-operative heart rate and blood pressure.

2.2. Transfusion-related cost calculations

All costs were calculated as of 30 June 2017. Transfusion-related costs were calculated as allogeneic transfusion cost + ICS setup cost + ICS reinfusion cost. Costs related to length of hospital stay and complications were not included.

Allogeneic transfusion costs include both the product cost of each RBC unit and the process costs. The product cost of AUD $412.66 per unit was determined by the current listings of the National Blood Authority, Australia [43], after confirming these were the prices currently paid by our institution. Process costs of transfusion, including in-hospital logistics, blood tests, staffing and overhead expenses, are known to be three to five times higher than the product cost of the unit of blood itself [12,13]. These have previously been used in Australia to calculate more comprehensive estimates of the cost of transfusion [44,45]. The first estimate of process costs in Australia by Wood et al. [44] in 2006 of AUD $370 per unit of RBC infused were updated by Leahy and Mukhtar [45] in 2010 to AUD $536 using the Australian Bureau of Statistics consumer price index for hospital and medical services. Utilising the same method translated to a subsequent 45.3% increase from end-of-financial-year 2010 to 2017, giving a current process cost of AUD $779 [46], and a total cost per unit of RBC infused of AUD $1191.66.

To calculate ICS costs, every equipment item used during ICS was systematically listed and its current replacement price obtained from the theatre logistics department. ICS staffing costs were included, and represent the majority of the ICS setup cost. The machine is run by one of several dedicated ICS-trained in-house year $\geq$9 anaesthetic nurse. When ICS is electively requested, the practice of our institution is to roster an additional anaesthetic nurse to liberate one who is ICS trained. Due to a limited in-house staffing pool, it is often necessary to hire an agency nurse for this purpose. Current pricing in our institution for an in-house year $\geq$9 anaesthetic nurse is AUD $42.28 per hour for a set 8 h shift, and for an equivalent agency nurse AUD $77 per hour for a flexible duration shift. Of the ICS cases, seven utilised in-house nurse cover totalling 56 h, while for nine an agency nurse was employed for 70.75 h in all. This represented a total ICS staffing cost of $7815.43, or $488.46 per ICS case. Incorporating this, ICS setup cost was AUD $609.85 per case, with reinfusion costing an additional AUD $382.00 per case (Table 1).

2.3. Statistical analysis

Continuous data were summarized as medians with interquartile range (IQR), and significance assessed using the Wilcoxon (Mann–Whitney) test. Categorical measures were summarized as proportions and assessed with Pearson's chi-square test. All tests were two-tailed and significance was assessed at the 5% alpha level. Data were analysed using SAS v9.3 (SAS Institute Inc., Cary, NC, USA).

3. Results

3.1. Demographics and surgical approach

Forty patients underwent open nephrectomy for suspected malignancy during the enrolment period. Sixteen patients received ICS (ICS group) while 24 did not (standard group) (Table 2). The ICS group had similar median age (63.5 *vs.* 61.0 years, $p = 0.83$) but a lower proportion of females (19% *vs.* 58%, $p = 0.013$). Median pre-operative (144 *vs.* 139 g/L, $p = 0.99$), post-operative haemoglobin (120 *vs.* 112 g/L, $p = 0.86$) and median Charlson Comorbidity Index (4 *vs.* 3, $p = 0.35$) were comparable.

The groups had similar proportions with left-sided tumours (44% *vs.* 42%, $p = 0.90$) and thoracoabdominal approach (88% *vs.* 79%, $p = 0.50$). Other approaches for the ICS and standard group were midline laparotomy (one and three cases respectively) and subcostal chevron incision (one and two cases respectively). The ICS group had a higher proportion of radical rather than partial nephrectomy (81% *vs.* 46%, $p = 0.025$) and shorter median follow-up (278 *vs.* 827 days, $p = 0.0005$).

Table 1 The cost of ICS set-up and reinfusion in Australian dollars, as of 30 June 2017.

Cost ($)	Item
0.98	Separate Yanker sucker
27.50	Dual lumen sucker line
12.64	Anticoagulant; 2 ampoules of 25 000 units/5 mL heparin
2.13	ICS machine tubing
1.10	1 × 1000 mL 0.9% normal saline
72.50	ICS reservoir
4.54	Bacterial filter
488.46	Anaesthetic nurse wages per case
609.85	Sub-total, ICS setup cost
56.00	Leucocyte depletion filter; Haemonectics™ RS1VAE
280.00	ICS processor set
35.00	Reinfusion bag
11.00	10 × 1000 mL 0.9% normal saline per 500 mL reinfused @ $1.10/bag
382.00	Sub-total, ICS reinfusion cost

ICS, intra-operative cell salvage.

Table 2 Patient demographics and surgical approach.

Index	ICS	Standard	*p*-Value
Demographics			
Patients (n)	16	24	
Age (year), median (IQR)	63.5 (56–70)	61 (51–71)	0.83
Female, *n* (%)	3 (19%)	14 (58%)	0.013
Pre-operative haemoglobin (g/L), median (IQR)	144 (114–152)	139 (133–149)	0.99
Post-operative haemoglobin (g/L), median (IQR)	120 (95–127)	112 (101–125)	0.86
Charlson Comorbidity Index, median (IQR)	4 (2–5)	3 (2–5)	0.35
Length of stay (day), median (IQR)	7 (5–7)	7 (6–9)	0.42
Follow-up (day), median (IQR)	278 (130–554)	827 (549–1319)	0.0005
Approach			
Thoracoabdominal, *n* (%)	14 (88%)	19 (79%)	0.50
Left-sided tumour, *n* (%)	7 (44%)	10 (42%)	0.90
Radical, *n* (%)	13 (81%)	11 (46%)	0.025

ICS, intra-operative cell salvage; IQR, interquartile range.

3.2. Histology

Fourteen ICS patients and 15 standard patients had histologically confirmed renal cancer (Table 3). The tumour type was clear cell renal cell carcinoma (RCC) for 12 and 11 patients in the ICS and standard groups respectively. Other histological types in the ICS group were one case each of chromophobe and papillary RCC, while in the standard group there were three cases of papillary RCC and one of large cell undifferentiated urothelial carcinoma. The number of patients with pathological tumour stage T1, T2 and T3 was three, four and seven in the ICS group and ten, one and three in the standard group respectively. Significantly more ICS patients had stage $\geq$T2 disease (79% *vs.* 27%; $p = 0.005$). Both groups had one patient with nodal stage N1, while three ICS patients and one standard patient had metastasis detected pre-operatively. These represented six separate patients.

3.3. Intra-operative cell salvage use

Of the 16 patients in the ICS group for whom lost blood was collected, five (31%) had salvaged blood reinfused. The median volume returned was 276 mL (IQR: 223–536 mL).

3.4. Primary outcomes

One patient each in the ICS and standard groups received allogeneic transfusion (6% *vs.* 4%). These patients had pre-operative haemoglobin of 101 g/L and 117 g/L, and had two and one units given respectively. Amongst patients with histologically confirmed malignancy without evidence of metastasis pre-operatively, tumour recurrence rates were similar (18% *vs.* 7%, $p = 0.40$). Two patients recurred in the ICS group. The first had a T2aN0 100 mm RCC while the second had a T3aN1 115 mm RCC. The sole standard group patient with recurrence had an 85 mm T3aN1 large cell undifferentiated urothelial carcinoma. All three cases had negative surgical margins, and were resected radically. The two patients with N1 disease were the study's only instances of nodal positivity.

3.5. Secondary outcomes

Complication rates were comparable (19% *vs.* 29%; $p = 0.46$) (Tables 3 and 4). There were no deaths during the index admission, and no TTIs. Regarding price estimation, machine set-up costs applied to all ICS patients, of whom five used further resources through reinfusion. Calculating total transfusion-related costs as allogeneic transfusion cost + ICS setup cost + ICS reinfusion cost, the ICS group's costs were AUD \$14 050.92 (\$2383.32 + \$9757.60 + \$1910.00) compared with AUD \$1191.66 for the standard group (\$1191.66 + \$0 + \$0). Correspondingly, per capita transfusion-related costs were markedly higher in the ICS group (AUD \$878.18 *vs.* \$49.65 per patient) (Table 3).

Analyses were re-run with patients segregated by partial or radical surgical approach, comparing those with and without ICS use. Results were unchanged, with no statistical difference for ATRs, recurrence and complications (data not shown).

4. Discussion

The literature to date regarding ICS use in urology is restricted to a collection of case reports and case series, and 14 comparative cohort studies [19,26,29–38,41,47], with no grade I or II evidence. Our study represents the first comparative study of ICS to include radical nephrectomy and the first in any urological procedure outside the UK and the USA. It is also only the fourth comparative study of ICS in any specialty in Australia [48–50].

ATRs were low at 4%–6%, regardless of ICS use, representing only one patient in each group. This was an unexpected finding, and below published norms for open partial (5%–30%) [3–6] and radical nephrectomy (18%–45%) [3,5,7]. It is also below the 8%–21% ATRs reported in Lyon et al.'s analysis [38] of ICS in partial nephrectomy. Causes for this low transfusion rate are likely to be multi-factorial, including the favourable Charlson Comorbidity Index and pre-operative haemoglobin, and the high degree of renal hilar control afforded by the thoracoabdominal approach. Both patients requiring transfusion had low starting haemoglobin

Table 3 Histopathology and outcomes.

Index	ICS ($n = 16$)	Standard ($n = 24$)	p-Value
Histology [a]			
Malignant	14	15	
Renal cell carcinoma, *n* (%)	12 (86)	11 (73)	N/A
Size (mm), median (IQR)	63 (31–111)	27 (22–69)	0.11
Margin positive, *n* (%)	0 (0)	0 (0)	N/A
Tumour stage ≥T2, *n* (%)	11 (79)	4 (27)	0.005
Nodal stage N1, *n* (%)	1 (7)	1 (7)	1
Metastasis stage M1, *n* (%)	3 (21)	1 (7)	0.25
Outcomes [a]			
Patients with allogeneic transfusion, *n* (%)	1/16 (6)	1/24 (4)	0.96
Malignant and M0, disease recurrence, *n* (%)	2/11 (18)	1/14 (7)	0.40
Complications, *n* (%)	3/16 (19)	7/24 (29)	0.46
Transfusion-related cost (AUD, $)	878.18	49.65	N/A

AUD, Australian dollars; ICS, intra-operative cell salvage; IQR, interquartile range; M0, no metastases detected pre-operatively; N/A, not applicable.

[a] Percentages for histology and disease recurrence results used number of patients with malignant disease as the denominator. Percentages for all other outcomes used total patients in group as the denominator.

Table 4 Complications.

	C-D grade	Patients and histology details
Intra-operative cell salvage group		
Self-limiting asymptomatic fever	1	62yr M CCI 4, 15 mm T1N0M0
Self-limiting asymptomatic hyperkalaemia	1	74yr M CCI 7, 60 mm T3N0M0
Persistent high drain outputs. Drain left *in-situ* on discharge and removed subsequently in outpatients	3a	74yr M CCI 9, 70 mm T3N0M1
Standard group		
Self-limiting asymptomatic fever	1	51yr M CCI 3, 70 mm T3N0M0
Self-limiting asymptomatic hypoxia	1	84yr F CCI 8, 85 mm T3N1M1
Post-operative ileus, resolved without nasogastric tube	1	69yr M CCI 4, 15 mm oncocytoma
Hospital acquired pneumonia + rotavirus-positive diarrhea, treated with antibiotics and supported therapy	2	66yr M CCI 3, 28 mm oncocytoma
Angina pectoris with normal investigations	2	70yr F CCI 5, 37 mm T1N0M0
Small pneumothorax post-underwater sealed drain removal; resolved with conservative management	3a	88yr F, CCI 5, benign atrophic kidney
Intra-operative laceration to proximal ureter anterior wall during partial nephrectomy, managed with ureteric stent for 6 weeks	3a	71yr M CCI 3, 22 mm T1N0M0

CCI, Charlson Comorbidity Index; C-D, Clavien-Dindo; F, female; M, male; TNM, tumour node metastasis stage; yr, year.

concentration, highlighting the importance of pre-operative optimisation including correction of anaemia.

Both groups had similar low rates of tumour recurrence, being present in two ICS patients and one standard patient. This is consistent with the results of Lyon et al. [38], as well as comparative studies of prostatectomy and cystectomy, all of which found recurrence in ICS patients was equivalent to [29–33,35,36] or less than controls [34,37]. This finding was the more reassuring given the less favourable oncological characteristics amongst our ICS group, with larger, higher stage tumours. The groups also had comparable complication rates, in line with many other studies supporting the safety of ICS in uro-oncology [19,33,38,41,47].

Three studies to date have reported cost analyses for ICS in urology. All were retrospective cohort studies. In 1995, Gilbert et al.'s USA-based study [26] reported 172 patients undergoing radical retrograde prostatectomy. Half utilised PAD and ICS, with the remainder receiving PAD only. They found transfusion-related costs were greater in the ICS group, at USD $1409 *vs.* $976 per patient. Two more recent UK studies published in 2010 and 2011 comparing ICS to no blood conservation technique found the reverse. An analysis of 30 patients undergoing radical cystectomy noted lower costs in the ICS group, at UK Pounds (UKP) £320 *vs.* £675 [19]. Similar savings were reported in another study of 50 men receiving radical retrograde prostatectomy (UKP £163 *vs.* £372) [35].

ICS was not cost effective for open nephrectomy in our institution. The two main contributors to this finding were the surprisingly low ATRs and the high staffing cost of ICS.

Published indications for ICS use are elective or emergency surgery where the estimated blood loss is >20% of total blood volume, induces anaemia or requires transfusion in >10% of patients [42,51]. The ATRs observed in this study were below this level, limiting the potential benefits of ICS. The use of casual agency staff to liberate in-house ICS-trained anaesthetic nurses was also more expensive than anticipated. Additionally, in most ICS cases reinfusion did not occur, with the dedicated ICS anaesthetic nurse largely unoccupied after machine setup. Driven by these results, our department is taking steps to reduce these costs. These include creation of a larger pool of in-house anaesthetic nurses, and negotiations with a more competitively priced nursing agency. Additionally, we are exploring modifying ICS operational practice, with the machine potentially becoming a responsibility of the pre-existing anaesthetic nurse, who is present for all cases alongside an anaesthetist, regardless of ICS use. This may remove ICS-specific staffing costs altogether.

We believe that in sites with similar allogeneic transfusion and ICS costs and no separate ICS staffing, ICS will reduce transfusion-related costs only for procedures with expected transfusion rates >50%. Future advances in ICS technology may improve its cost effectiveness, by reducing setup costs, and returning a higher proportion of shed blood.

This study is limited by its retrospective nature, small size, non-randomised nature and short follow-up. Differences between groups, the principal feature of non-randomised studies, were significant for important characteristics such as tumour stage, and this selection bias may have impacted our findings.

5. Conclusion

ICS use in open nephrectomy appears safe, with similar tumour recurrence and complications compared to the standard group. ATRs were unexpectedly low in both groups. Therefore, ICS was not cost effective for open nephrectomy in our institution. ICS use may offer greater cost benefit when used in urological centres or procedures with higher ATRs. Larger and prospective studies are required to confirm these findings.

Author contributions

Study design: Ned Kinnear
Data acquisition: Ned Kinnear, Lina Hua, Bridget Heijkoop
Data analysis: Ned Kinnear, Lina Hua, Bridget Heijkoop
Drafting of manuscript: Ned Kinnear
Critical revision of the manuscript: Ned Kinnear, Lina Hua, Bridget Heijkoop, Derek Hennessey, Daniel Spernat

Conflicts of interest

The authors declare no conflict of interest.

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References

[1] Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer 2015;136:E359—86.
[2] Dy GW, Gore JL, Forouzanfar MH, Naghavi M, Fitzmaurice C. Global burden of urologic cancers, 1990—2013. Eur Urol 2017; 71:437—46.
[3] Shvarts O, Tsui KH, Smith RB, Kernion JB, Belldegrun A. Blood loss and the need for transfusion in patients who undergo partial or radical nephrectomy for renal cell carcinoma. J Urol 2000;164:1160—3.
[4] Gill IS, Kavoussi LR, Lane BR, Blute ML, Babineau D, Colombo Jr JR, et al. Comparison of 1,800 laparoscopic and open partial nephrectomies for single renal tumors. J Urol 2007;178:41—6.
[5] MacLennan S, Imamura M, Lapitan MC, Omar MI, Lam TB, Hilvano-Cabungcal AM, et al. Systematic review of perioperative and quality-of-life outcomes following surgical management of localised renal cancer. Eur Urol 2012;62: 1097—117.
[6] Shen Z, Xie L, Xie W, Hu H, Chen T, Xing C, et al. The comparison of perioperative outcomes of robot-assisted and open partial nephrectomy: a systematic review and meta-analysis. World J Surg Oncol 2016;14:220.
[7] Bragayrac LA, Abbotoy D, Attwood K, Darwiche F, Hoffmeyer J, Kauffman EC, et al. Outcomes of minimal invasive *vs* open radical nephrectomy for the treatment of locally advanced renal-cell carcinoma. J Endourol 2016;30: 871—6.
[8] Bolton-Maggs PHB, Poles D. SHOT Group. Annual SHOT Report 2016 [Internet]. 2017 [Accessed 1 September 2017]. Available from: https://www.shotuk.org/wp-content/uploads/SHOT-Report-2016_web_11th-July.pdf.
[9] US Food and Drug Administration. Fatalities Reported to FDA Following Blood Collection and Transfusion Annual Summary for FY2015 [Internet]. 2015 [Accessed 1 September 2017]. Available from: https://www.fda.gov/downloads/BiologicsBloodVaccines/SafetyAvailability/ReportaProblem/TransfusionDonationFatalities/UCM518148.pdf.
[10] Funk MB, Heiden M, Volkers P, Lohmann A, Keller-Stanislawski B. Evaluation of risk minimisation measures for blood components - based on reporting rates of transfusion-transmitted reactions (1997-2013). Transfus Med Hemotherapy 2015;42:240—6.
[11] Sun T, Lu SF, Jin GZ. Solving shortage in a priceless market: insights from blood donation. J Health Econ 2016;48:149—65.
[12] Shander A, Hofmann A, Ozawa S, Theusinger OM, Gombotz H, Spahn DR. Activity-based costs of blood transfusions in surgical patients at four hospitals. Transfusion 2010;50:753—65.
[13] Leahy MF, Trentino KM, May C, Swain SG, Chuah H, Farmer SL. Blood use in patients receiving intensive chemotherapy for acute leukemia or hematopoietic stem cell transplantation: the impact of a health system-wide patient blood management program. Transfusion 2017;57:2189—96.
[14] Soubra A, Zabell JR, Adejoro O, Konety BR. Effect of perioperative blood transfusion on mortality for major urologic malignancies. Clin Genitourin Cancer 2015;13:e173—81.

[15] Vamvakas EC, Blajchman MA. Transfusion-related immunomodulation (TRIM): an update. Blood Rev 2007;21:327—48.
[16] Davies L, Brown TJ, Haynes S, Payne K, Elliott RA, McCollum C. Cost-effectiveness of cell salvage and alternative methods of minimising perioperative allogeneic blood transfusion: a systematic review and economic model. Health Technol Assess 2006;10:1—210. iii-iv, ix-x.
[17] Carless PA, Henry DA, Moxey AJ, O'Connell D, Brown T, Fergusson DA. Cell salvage for minimising perioperative allogeneic blood transfusion. Cochrane Database Syst Rev 2010. https://doi.org/10.1002/14651858. CD001888.
[18] Brecher ME, Goodnough LT. The rise and fall of preoperative autologous blood donation. Transfusion 2001;41:1459—62.
[19] Ubee SS, Manikandan R, Gudimetla AR, Singh G. Cost benefits of intraoperative cell salvage in radical cystectomy. Indian J Urol 2010;26:196—9.
[20] Shin HJ, Na HS, Do SH. The effects of acute normovolaemic haemodilution on peri-operative coagulation in total hip arthroplasty. Anaesthesia 2015;70:304—9.
[21] Carson JL, Triulzi DJ, Ness PM. Indications for and adverse effects of red-cell transfusion. N Engl J Med 2017;377:1261—72.
[22] Kuppurao L, Wee M. Perioperative cell salvage. Continuing education in anaesthesia. Critical Care Pain 2010;10:104—8.
[23] Linden J. Autologous blood errors and incidents (abstract). In: American Association of blood banks 47 annual meeting november 12—17, 1994: Transfusion; 1994. 28S.
[24] Domen RE. Adverse reactions associated with autologous blood transfusion: evaluation and incidence at a large academic hospital. Transfusion 1998;38:296—300.
[25] DeAndrade D, Waters JH, Triulzi DJ, Alarcon L, Wisniewski MK, Dyga R, et al. Very low rate of patient-related adverse events associated with the use of intraoperative cell salvage. Transfusion 2016;56:2768—72.
[26] Gilbert JB, Malkowicz SB, Wein AJ. Cell saver and radical retropubic prostatectomy: analysis of cost-effectiveness. Urology 1995;46:542—4.
[27] Yaw PB, Sentany M, Link WJ, Wahle WM, JL GG. Tumor cells carried through autotransfusion. Contraindication to intraoperative blood recovery? JAMA 1975;231:490—1.
[28] Waters JH, Yazer M, Chen YF, Kloke J. Blood salvage and cancer surgery: a meta-analysis of available studies. Transfusion 2012;52:2167—73.
[29] Gray CL, Amling CL, Polston GR, Powell CR, Kane CJ. Intraoperative cell salvage in radical retropubic prostatectomy. Urology 2001;58:740—5.
[30] Davis M, Sofer M, Gomez-Marin O, Bruck D, Soloway M. The use of cell salvage during radical retropubic prostatectomy: does it influence cancer recurrence? BJU Int 2003;91:474—6.
[31] Nieder AM, Carmack AJ, Sved PD, Kim SS, Manoharan M, Soloway MS. Intraoperative cell salvage during radical prostatectomy is not associated with greater biochemical recurrence rate. Urology 2005;65:730—4.
[32] 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—5.
[33] Nieder AM, Manoharan M, Yang Y, Soloway MS. Intraoperative cell salvage during radical cystectomy does not affect long-term survival. Urology 2007;69:881—4.
[34] MacIvor D, Nelson J, Triulzi D. Impact of intraoperative red blood cell salvage on transfusion requirements and outcomes in radical prostatectomy. Transfusion 2009;49:1431—4.
[35] Ubee S, Kumar M, Athmanathan N, Singh G, Vesey S. Intraoperative red blood cell salvage and autologous transfusion during open radical retropubic prostatectomy: a cost-benefit analysis. Ann R Coll Surg Engl 2011;93:157—61.
[36] Gorin MA, Eldefrawy A, Manoharan M, Soloway MS. Oncologic outcomes following radical prostatectomy with intraoperative cell salvage. World J Urol 2012;30:379—83.
[37] Raval JS, Nelson JB, Woldemichael E, Triulzi DJ. Intraoperative cell salvage in radical prostatectomy does not appear to increase long-term biochemical recurrence, metastases, or mortality. Transfusion 2012;52:2590—3.
[38] Lyon TD, Ferroni MC, Turner 2nd RM, Jones C, Jacobs BL, Davies BJ. Short-term outcomes of intraoperative cell saver transfusion during open partial nephrectomy. Urology 2015;86:1153—8.
[39] Kassouf W, Siemens R, Morash C, Lacombe L, Jewett M, Goldenberg L, et al. Follow-up guidelines after radical or partial nephrectomy for localized and locally advanced renal cell carcinoma. Can Urol Assoc J. 2009;3:73—6.
[40] Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205—13.
[41] Waters JH, Lee JS, Klein E, O'Hara J, Zippe C, Potter PS. Preoperative autologous donation versus cell salvage in the avoidance of allogeneic transfusion in patients undergoing radical retropubic prostatectomy. Anesth Analg 2004;98:537—42.
[42] Esper SA, Waters JH. Intra-operative cell salvage: a fresh look at the indications and contraindications. Blood Transfus 2011;9:139—47.
[43] National Blood Authority Australia. What Blood Products are Supplied—National Product List [Internet]. 2017 [Accessed 1 September 2017], https://www.blood.gov.au/national-product-list.
[44] Wood E, Bielby L, Hunt R, Peterson D, Roxby D, et al. Transfusing a Unit of Red Cells—What Does It Really Cost in Australia?. In: proceedings of the Haematology Society of Australia and New Zealand Annual Scientific Meeting; 2008. Perth, Australia.
[45] Leahy M, Mukhtar S. From blood transfusion to patient blood management: a new paradigm for patient care and cost assessment of blood transfusion practice. Intern Med J 2012;42:332—8.
[46] Australian Bureau of Statistics. Consumer price index, hospital and medical services; Australia (A2329041T) [Internet]. 2017 [Accessed 1 September 2017], http://www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/6401.0Sep 2017?OpenDocument Time.
[47] Chiusano M, Finkelstein L, Mene M, Ginsberg P. Use of predeposited autologous blood plus intraoperative autotransfusion compared with use of predeposited autologous blood alone in radical retropubic prostatectomy. J Am Osteopath Assoc 1996;96:160—4.
[48] McDonnell NJ, Kennedy D, Long LJ, Gallagher-Swann MC, Paech MJ. The development and implementation of an obstetric cell salvage service. Anaesth Intensive Care 2010;38:492—9.
[49] Gardner A, Gibbs N, Evans C, Bell R. Relative cost of autologous red cell salvage versus allogeneic red cell transfusion during abdominal aortic aneurysm repair. Anaesth Intensive Care 2000;28:646—9.
[50] Dan M, Liu D, Martos SM, Beller E. Intra-operative blood salvage in total hip and knee arthroplasty. J Orthop Surg (Hong Kong) 2016;24:204—8.
[51] National Blood Authority Australia. Guidance for the provision of intraoperative cell salvage [Internet]. 2014 [Accessed 1 September 2017], https://www.blood.gov.au/system/files/documents/ics-guidance-march-2014_1.pdf.