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Patient and disease factors predictive of adverse perioperative outcomes after nephrectomy

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ABSTRACT

INTRODUCTION The aim of this study was to determine the patient and disease factors predictive of adverse perioperative outcomes after nephrectomy using the British Association of Urological Surgeons (BAUS) audit database.

METHODS All nephrectomies entered on the BAUS database for the year 2012 were included and ten patient or disease factors were selected for analysis. Logistic regression was used to calculate the area under the receiver operating characteristic curve (AUC) (0.5 = no better than chance, 1.0 = perfect prediction) for each variable and 500 bootstrap samples were used to determine variable selection.

RESULTS Data were captured for 6,031 nephrectomies in 2012. World Health Organization performance status (WHO-PS) (AUC: 0.733) and anaemia (AUC: 0.696) were the most significant predictors of 30-day mortality in univariate analysis. WHO-PS (AUC: 0.626) and anaemia (AUC: 0.590) also predicted complications classified as Clavien–Dindo grades III–V. Anaemia (AUC: 0.722) and clinical T stage (AUC: 0.713) predicted need for transfusion.

CONCLUSIONS Adverse perioperative outcomes after nephrectomy are predicted by clinical presentation with haematuria, poor WHO-PS and higher TNM (tumour, lymph nodes, metastasis) stage. This study used surgeon collected data as opposed to an administrative database, which may have advantages in terms of accuracy and breadth of data fields. These data form a basis for preoperative patient counselling and informed consent for nephrectomy. They can also be used as a standard against which surgeons and hospitals can compare their own results.

KEYWORDS
Mortality – Complications – Transfusion – Nephrectomy – Outcomes

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Nephrectomy is indicated for a wide range of benign and malignant conditions. It encompasses simple, donor, radical and partial nephrectomy as well as nephroureterectomy. Nephrectomy carries an appreciable risk of morbidity and mortality, and these may be used as outcome measures for research and quality assurance purposes.

Mortality, complication rate and need for blood transfusion are three outcomes that may be used as a benchmark for nephrectomy. The mortality rate after nephrectomy can be expressed in a number of ways. Thirty-day mortality is a well recognised measure, and a rate of 0.9% for over 24,000 patients from the US National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) database has been described.[1] Ninety-day mortality is an alternative measure and a rate of 4.4% for nephroureterectomy has been observed.[2] Complications after nephrectomy can be reported on the standardised Clavien–Dindo scoring system[3] and a rate of 12% has been shown.[4] The blood transfusion rate from a national database was 18.1%.[5]

The British Association of Urological Surgeons (BAUS) nephrectomy database was launched in 2001 to collect surgeon reported outcome data. Data submission was voluntary. Based on a comparison between BAUS data and the Hospital Episode Statistics (HES) database for National Health Service (NHS) trusts, the capture rate remained at around 30%. Mandatory reporting of mortality and quality outcomes was introduced by the NHS in 2012, and nephrectomy was chosen as the first procedure for which data would be published. The capture rate is now estimated to have increased to 80%. The perioperative outcomes for 2012 showed a 30-day mortality rate of 0.56%, a complication rate of 4.0% (Clavien–Dindo grades III–V) and a blood transfusion rate of 8.5%.[6] Although informative, these rates vary substantially depending on patient and disease factors.

Analysis of large series of nephrectomies has been carried out to determine the predictors of adverse outcomes. The low event rate of mortality, morbidity and transfusion for nephrectomy means that in order to obtain sufficient numbers of operations for logistical regression analysis, interrogation of large databases is required. Examples of these include the HES database in England and data from the SEER programme in the US. HES data are used to record clinical activity and pay hospitals for the care that they deliver. They are not designed to record clinical outcomes; the coding is performed retrospectively by non-clinicians and may be inaccurate.[7] The aim of this study was to examine the patient and disease factors that most accurately predict adverse perioperative outcomes for nephrectomy using a large database with surgeon reported data.

Methods

All data recorded on the BAUS nephrectomy database for the year 2012 were included for analysis. This year was chosen because the higher capture rate could potentially limit reporting bias. The data were divided into five nephrectomy types: simple nephrectomy, partial nephrectomy, radical nephrectomy, nephroureterectomy and other. Analysis of the data was attempted in these subgroups but this resulted in a low or zero number of patients and events in many categories. This division was therefore reversed and all nephrectomies were analysed together. The variables 'M stage' and 'cytoreductive surgery' were combined into one category. Three perioperative outcomes (30-day mortality, complications and blood transfusion) were selected for analysis.

Data refinement

Patients with the T stage recorded as 'in situ' were excluded (n=2). For patients whose T stage was recorded as 0 but who had undergone partial or radical nephrectomy, or nephroureterectomy, T stage was changed to 'missing' (n=24). Patients whose T stage was recorded as 'a' were recoded as T1a (n=75). For those whose procedure was listed as 'not recorded', this was set to 'missing' (n=45).

The outcome variable '30-day mortality' was coded as either 'yes' or 'no'. Patients with N stage 3 were excluded from 30-day mortality analysis as there were only 6 patients in this group and no recorded deaths. Clavien–Dindo grade for complications was converted into the dichotomous variable 'CD ≥III' and coded as either 'yes' or 'no'. Similarly, 'units of blood transfused' was converted into the dichotomous variable 'blood transfusion' and coded as either 'yes' or 'no'.

The variable 'postoperative complications' was used to determine missing data for Clavien–Dindo grade. If a patient had 'no' recorded for this variable, he or she was assumed to truly have no complications and was therefore coded as 'CD ≥III = no'. On the other hand, if a patient had 'yes' recorded for the variable 'postoperative complications' but nothing was recorded for Clavien–Dindo grade, he or she was deemed to have missing data as it was not possible to determine whether any complications would be classified as higher or lower than grade III.

Statistical techniques

The BAUS database contains a possible 86 data fields for each nephrectomy but many of these are administrative (eg patient hospital number) or appear as additional questions in response to specific answers. (For example, if previous answers indicate that the tumour was in the supradiaphragmatic inferior vena cava, then the surgeon would be asked whether cardiopulmonary bypass was used). These data fields were analysed and any variables that might influence outcome were selected. These included sex, clinical presentation, World Health Organization performance status (WHO-PS), clinical T, N and M stages, serum haemoglobin, serum creatinine, patient age and procedure type.

Univariate logistic regression was used to determine the association of each variable with the outcome, and the area under the receiver operating characteristic curve (AUC) and p-value were calculated for each variable. The AUC was used to evaluate discrimination, showing how well the model identifies patients who experienced the outcome and those who did not.[8] An AUC of 1.0 would indicate that the model provides perfect prediction while 0.5 would mean that the model's prediction is no better than chance.

Bootstrapping was used to create 500 datasets by randomly selecting patients with replacement from the BAUS dataset. A backwards stepwise variable selection procedure was applied to each bootstrap dataset, for each of the outcomes (30-day mortality, transfusion and complications) separately. The percentage of times a variable was selected by the variable selection procedure in the 500 bootstrapped datasets (bootstrap inclusion frequency [BIF]) was used to identify those variables with the strongest association with outcome. Variables with a BIF of ≥50% were included in the final multivariate logistic regression model for each outcome. All statistical tests were performed using Stata® version 12 (StataCorp, College Station, TX, US).

Ethical approval

Patient data was encrypted and anonymised at national level before analysis. This project conformed to the definition of 'audit' by the NHS Health Research Authority and as such, ethical approval was not required.[9]

Results

In 2012 data were captured for 6,031 nephrectomies. The 30-day mortality rate was 0.6% (34/6,031). Table 1 shows the association of each variable with 30-day mortality. WHO-PS, serum haemoglobin and age were identified as the strongest univariate predictors of 30-day mortality.

Complications classified as Clavien–Dindo grades III–V occurred in 4.0% of cases with data (223/5,510). Table 2 shows the association of each variable with postoperative complications. WHO-PS and serum haemoglobin were identified as the strongest univariate predictors of postoperative complications.

A total of 8.5% (442/5,227) of all patients with data received a blood transfusion during admission. Table 3 shows the association of each variable with need for blood

Table 1 Univariate association and predictive ability for 30-day mortality after nephrectomy (*n*=6,031)

Variable	*n*	*p*-value	AUC
WHO-PS	4,922 (81.6%)	**<0.001**	0.733
Serum haemoglobin	4,783 (79.3%)	**<0.001**	0.696
Age	5,974 (99.1%)	**<0.001**	0.684
Clinical presentation	5,425 (90.0%)	**0.013**	0.650
Procedure	5,986 (99.3%)	**0.024**	0.648
Clinical T stage	5,197 (86.2%)	0.172	0.598
Clinical N stage	5,278 (87.5%)	0.149	0.568
Clinical M stage	5,306 (88.0%)	0.193	0.547
Serum creatinine	4,811 (79.8%)	0.198	0.544
Sex	5,976 (99.1%)	0.939	0.503

AUC = area under the curve; WHO-PS = World Health Organization performance status

Table 3 Univariate association and predictive ability for need for blood transfusion during admission for nephrectomy (*n*=6,031)

Variable	*n*	*p*-value	AUC
Serum haemoglobin	4,293 (71.2%)	**<0.001**	0.722
Clinical T stage	4,680 (77.6%)	**<0.001**	0.713
WHO-PS	4,509 (74.8%)	**<0.001**	0.614
Procedure	5,214 (86.5%)	**<0.001**	0.609
Clinical N stage	4,707 (78.0%)	**<0.001**	0.606
Clinical presentation	4,858 (80.6%)	**<0.001**	0.599
Clinical M stage	4,686 (77.7%)	**<0.001**	0.595
Serum creatinine	4,302 (71.3%)	**0.022**	0.575
Age	5,178 (85.9%)	**<0.001**	0.574
Sex	5,197 (86.2%)	0.106	0.520

AUC = area under the curve; WHO-PS = World Health Organization performance status

transfusion. Serum haemoglobin and clinical T stage were identified as the strongest univariate predictors of blood transfusion.

Bootstrapping

A logistic regression model with 500 bootstraps was used to determine the variable selection for the odds of experiencing each of the 3 adverse outcomes after nephrectomy. Owing to strong correlations between clinical T, N and M stages, multivariate models including each of these variables in turn were utilised. Variable selection for 30-day mortality and postoperative complications was the same across the models but slight differences were observed for transfusion. Table 4 shows whether variables were selected in more than 50% of the bootstrap samples. The variables WHO-PS, clinical presentation, and clinical T, N and M stages were all selected in over 50% of bootstrap samples, indicating prognostic ability.

Table 2 Univariate association and predictive ability for postoperative complications after nephrectomy (*n*=6,031)

Variable	*n*	*p*-value	AUC
WHO-PS	4,772 (79.1%)	**<0.001**	0.626
Serum haemoglobin	4,475 (74.2%)	**<0.001**	0.590
Procedure	5,488 (91.0%)	**0.022**	0.564
Age	5,434 (90.1%)	**0.002**	0.559
Clinical T stage	4,859 (80.6%)	**0.025**	0.549
Serum creatinine	4,524 (75.0%)	**0.049**	0.546
Clinical presentation	5,069 (84.0%)	0.056	0.543
Clinical M stage	4,977 (82.5%)	**0.003**	0.543
Clinical N stage	4,900 (81.2%)	0.135	0.531
Sex	5,457 (90.5%)	0.919	0.502

AUC = area under the curve; WHO-PS = World Health Organization performance status

Odds ratios

Univariate odds ratios and confidence intervals for patient and disease variables are shown in Tables 5 and 6. In general, there was an increasing risk of adverse outcome with increasing WHO-PS, increasing age, lower haemoglobin and 'other' or 'haematuria' versus 'incidental' presentation preoperatively. The odds ratios associated with serum creatinine and sex were not significant for any of the models. The smaller confidence intervals for haemoglobin, age, creatinine and sex are due to these being applicable for all nephrectomies whereas the larger confidence intervals for other categories reflect the smaller number of nephrectomies in each of these groups.

Discussion

The mandatory reporting of nephrectomy outcome data in England has provided a rich resource of surgeon collected data for interrogation. This study used these data to identify the patient and disease related factors that are most predictive of adverse perioperative outcomes for nephrectomy. The possible patient factors include age, sex, WHO-PS, serum haemoglobin, serum creatinine and clinical presentation. Patients with little physiological reserve who undergo the stress of major surgery are at increased risk of adverse perioperative outcomes, and this is reflected in the strong association between WHO-PS and 30-day mortality, complications and need for blood transfusion. Age showed a less strong association, and this may be due to some elderly patients being very fit and younger patients unfit.

Table 4 Bootstrap variable selection for adverse outcomes after nephrectomy

Variable	30-day mortality	Postoperative complications	Blood transfusion
WHO-PS	Yes	Yes	Yes
Clinical presentation	Yes	Yes	Yes
Clinical T stage	Yes	Yes	Yes
Clinical N stage	Yes	Yes	Yes
Clinical M stage	Yes	Yes	Yes
Serum haemoglobin	No	Yes	Yes
Procedure	No	Yes	Yes*
Age	No	No	Yes
Sex	No	No	Yes**
Serum creatinine	No	No	No

WHO-PS = World Health Organization performance status
*selected in multivariate models for clinical N and M stages;
**selected in multivariate model for clinical M stage

Unsurprisingly, low haemoglobin was associated with a high risk of blood transfusion but there was also a strong link with 30-day mortality and complications. Low haemoglobin is one of the five risk factors associated with shorter survival in metastatic renal cell carcinoma.[10] However, in a population-based study of disease free patients, high and low haemoglobin levels were found to have an independent prognostic effect on mortality.[11] A meta-analysis of 24 surgical studies also showed an increased postoperative mortality rate with anaemia (odds ratio: 2.90, 95% confidence interval: 2.30–3.68).[12] The aetiological reason for this is unclear, perhaps representing a surrogate marker for generalised ill health. Whether correction of preoperative anaemia improves postoperative mortality merits further investigation. Sex was shown consistently to be unassociated with outcome.

The disease factors include T, N and M stages and procedure type. It follows that an operation to remove a higher stage, more advanced disease is associated with an increased chance of adverse outcome. Nephroureterectomy is usually performed on a more elderly population, and results in a higher risk of mortality and complications but a lower risk of transfusion than radical nephrectomy.

Table 5 Univariate odds ratios for patient related factors and adverse outcomes after nephrectomy

Variable		30-day mortality		Blood transfusion		CD grades III–V	
		OR	95% CI	OR	95% CI	OR	95% CI
Clinical presentation	Incidental	1		1		1	
	Haematuria	4.40	1.61–12.03	2.59	1.96–3.41	1.41	0.99–2.03
	Other	2.44	0.85 – 7.03	2.47	1.88–3.24	1.47	1.04–2.06
WHO-PS	0	1		1		1	
	1	2.69	0.98–7.41	2.12	1.67–2.70	1.80	1.30–2.49
	2	9.89	3.69–26.46	2.94	2.16–4.00	3.15	2.14–4.62
	3	9.41	1.87–47.24	3.05	1.65–5.64	5.05	2.64–9.66
	4	29.17	3.31–257.24	1.60	0.20–12.48	11.35	3.58–36.04
Haemoglobin		0.97*	0.95–0.98*	0.96*	0.95–0.96*	0.98*	0.98–0.99*
Age		1.06**	1.03–1.09**	1.02**	1.01–1.03**	1.02**	1.01–1.03**
	<40 years	1		1		1	
	40–49 years	0.70	0.04–11.29	1.87	0.97–3.61	1.65	0.80–3.39
	50–59 years	2.17	0.25–18.59	2.97	1.64–5.40	1.26	0.63–2.53
	60–69 years	2.23	0.28–17.88	3.64	2.04–6.48	1.82	0.96–3.48
	70–79 years	3.38	0.43–26.45	3.69	2.06–6.61	2.20	1.15–4.20
	≥80 years	9.02	1.14–71.46	3.60	1.90–6.83	1.81	0.85–3.85
Creatinine		1.000***	0.999–1.005***	1.001***	1.000–1.002***	1.001***	1.0002–1.003***
Male sex		0.97	0.49–1.93	1.18	0.97–1.45	0.99	0.75–1.29

CD = Clavien–Dindo; OR = odds ratio; CI = confidence interval; WHO-PS = World Health Organization performance status
*for every 1g/l increase in haemoglobin; **for every one-year increase in age; ***for every 1μmol/l increase in creatinine

Table 6 Univariate odds ratios for disease related factors and adverse outcomes after nephrectomy

Variable		30-day mortality		Blood transfusion		CD grades III–V	
		OR	95% CI	OR	95% CI	OR	95% CI
Procedure	RN	1		1		1	
	SN	1.03	0.37–2.81	0.44	0.32–0.61	1.34	0.91–1.97
	PN	0.19	0.02–1.40	0.28	0.19–0.41	1.69	1.19–2.39
	NU	2.49	1.15–5.39	0.73	0.54–0.97	1.54	1.05–2.28
	Other	4.59	0.59–35.38	1.38	0.53–3.59	3.26	1.14–9.33
Clinical T stage	1	1		1		1	
	2	1.67	0.59–4.72	4.36	3.19–5.95	0.98	0.64–1.51
	3	1.87	0.62–5.60	7.54	5.53–10.29	1.44	0.94–2.22
	4	7.33	1.55–34.63	11.33	6.11–21.00	4.42	2.10–9.31
Clinical N stage	0	1		1		1	
	1	3.96	1.31–11.96	2.56	1.71–3.84	2.25	1.24–4.08
	2	1.08	0.14–8.16)	2.97	2.00–4.40	1.41	0.64–3.08
	3	No deaths	–	7.68	1.28–46.21	5.88	0.65–53.0
Clinical M stage	0	1		1		1	
	1	2.41	0.90–6.50	2.59	1.93–3.47	2.28	1.48–3.50

CD = Clavien–Dindo; OR = odds ratio; CI = confidence interval; RN = radical nephrectomy; SN = simple nephrectomy; PN = partial nephrectomy; NU = nephroureterectomy

In a study of over 24,000 patients on the SEER database, age and stage were found to be independent predictors of 30-day mortality after nephrectomy.[1] These variables could be combined to provide a model for predicting 30-day mortality after nephrectomy with around 80% accuracy. A similar study of over 6,000 patients on the SEER database demonstrated that age, T and N stages were predictors of 90-day mortality in nephroureterectomy.[2] However, the SEER dataset does not include information on co-morbidity or performance status.

In a multivariate analysis of patients undergoing nephrectomy for metastatic renal cell carcinoma, age and Karnofsky performance status were found to be most predictive of postoperative complications.[13] In our series, performance status was more predictive of complications than age and was selected in the bootstrapping model. For over 10,000 patients recorded on a Canadian discharge database, an overall transfusion rate of 18.1% was reported.[5] Multivariate logistic regression showed an association between age, Charlson co-morbidity index, procedure type, surgeon and hospital volume, and need for blood transfusion.

Our study has some limitations. The different types of nephrectomy were combined to allow statistical analysis of outcomes with low event rates. This meant that a higher number of cases could be analysed. Nevertheless, there is a disadvantage in that a partial nephrectomy for a small tumour is a very different operation to a nephrectomy with caval thrombectomy and that distinction is lost. Some refinement and simplification of data categories (complications and transfusion) was necessary to enable sufficiently powered statistical calculations. With increased amounts of data from subsequent years, subgroup analysis should be possible. The exclusion of some categories may have affected results adversely.

Surgeon collected data have the advantage of being entered largely by the clinician with direct responsibility for the patient, recording disease, patient and outcome data. The level of detail captured is far greater than that obtained from coding registry data. On the other hand, these data are subject to a reporting bias, with the possibility of adverse events not being recorded. Data from coding registries are collected routinely but may also be inaccurate as the information is not entered by clinicians and is used primarily for administrative purposes. The use of coding registry data (eg HES) to quality assure surgeon collected data is being explored.

Following the collection of data in 2012, feedback was requested from surgeons to refine the data categories used, and to accurately reflect the complexity of the disease and patient treated. As a result, a number of additional patient and disease data categories have now been included. The Charlson co-morbidity index and ASA (American Society of Anesthesiologists) grade were added, and it will be interesting to assess whether there is a stronger association with adverse outcomes with these rather than WHO-PS or other patient associated factors. A number of fields including body mass index, previous abdominal surgery, indication for partial nephrectomy and preoperative biopsy were also added to help stratify for factors that may make the operation more challenging.

Conclusions

This study used a large surgeon collected database to determine patient and disease factors predicting adverse outcomes after nephrectomy. The use of a surgeon reported database may have advantages over administrative databases in terms of accuracy and breadth of data categories although results must be interpreted with caution owing to possible reporting bias. It confirms the value of performance status and TNM (tumour, lymph nodes, metastasis) stage as predictors of adverse outcome after nephrectomy. Age showed a weaker correlation with outcome, suggesting that this should not be used in isolation to exclude patients from consideration for surgery. The strong association of anaemia with outcome requires further investigation. These data form a basis for patient counselling and informed consent before nephrectomy.

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