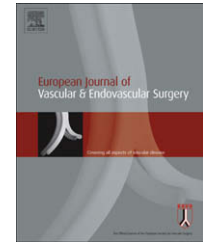




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The Development of a VBHOM-based Outcome Model for Lower Limb Amputation Performed for Critical Ischaemia[☆]

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KEYWORDS

Surgical audit;
Complications;
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Abstract *Background:* VBHOM (Vascular Biochemistry and Haematology Outcome Models) adopts the approach of using a minimum data set to model outcome and has been previously shown to be feasible after index arterial operations. This study attempts to model mortality following lower limb amputation for critical limb ischaemia using the VBHOM concept.

Methods: A binary logistic regression model of risk of mortality was built using National Vascular Database items that contained the complete data required by the model from 269 admissions for lower limb amputation. The subset of NVD data items used were urea, creatinine, sodium, potassium, haemoglobin, white cell count, age on and mode of admission. This model was applied prospectively to a test set of data ($n = 269$), which were not part of the original training set to develop the predictor equation.

Results: Outcome following lower limb amputation could be described accurately using the same model. The overall mean predicted risk of mortality was 32%, predicting 86 deaths. Actual number of deaths was 86 ($\chi^2 = 8.05$, 8 d.f., $p = 0.429$; no evidence of lack of fit). The model demonstrated adequate discrimination (c -index = 0.704).

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Conclusions: VBHOM provides a single unified model that allows good prediction of surgical mortality in this high risk group of individuals. It uses a small, simple and objective clinical data set that may also simplify comparative audit within vascular surgery.

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Introduction

Patients requiring lower limb amputation have a high associated peri-operative risk with reported 30-day mortality rates of up to 17%.¹ The high mortality rates observed in these patients are reflective of their multiple co-morbidities. Subjecting patients with a high operative risk to a futile operation has resource and ethical implications. Patient selection is usually dependent on the opinion and experience of the consultant vascular surgeon in conjunction with the anaesthetist. Therefore a scoring system that could identify patients pre-operatively in whom operative intervention would be unsuccessful would be valuable, but a reliable tool has yet to be found. It would be unjustifiable to deny a patient a potentially life-saving operation based on an inaccurate predictive instrument. A number of predictive factors associated with poor post-operative outcome after lower extremity amputation has been identified that could be used to stratify the operative risk.² These include female gender, congestive heart failure and high-level amputation. Statistical models have been built to accurately predict outcome after index arterial operations^{3–5} but these have generally suffered from incomplete data collection and have been too complex for practical regular use.

VBHOM (Vascular Biochemistry and Haematology Outcome Models) adopts a different approach of using a minimum data set to model outcome and has been previously shown to be feasible with index arterial operations.^{6–8} VBHOM uses only data items, which can be obtained pre-operatively. They are logistically feasible to collect from hospital pathology and patient administration computer systems and they are collected routinely within the normal pathways of clinical care. Importantly the clinical data are precisely measurable, objective and subject to the routine scrutiny of the hospital pathology department. In theory, these data items should be available for all patients. Therefore their application can be universal and data collection is not an additional burden to the staff providing care.

The aim of this study was to develop and validate a new VBHOM equation for patients undergoing lower limb amputation for critical ischaemia using data collected over an 8-year period from three hospitals within East Anglia, United Kingdom, of which one (Cambridge Vascular Unit) is an academic regional teaching centre.

Methods and Patients

The new VBHOM model was built from data collected on the National Vascular Database (NVD) amputation specific database form (http://www.vascularsociety.org.uk/Docs/Forms_VSGBI%20NVD%202006.pdf), from three hospitals within the East Anglia region, United Kingdom. Records

comprised of patients who underwent lower limb amputation for critical ischaemia from January 1998 to February 2006.

Indications for amputation were for dysvascularity only, including peripheral vascular disease (PVD), acute ischaemia, embolism and gangrene. A small number of these amputations were performed for ischaemic pain control and for long-standing non-healing ulceration. Patients who had lower amputations for trauma or for bone or lower limb tumours were excluded. Patients were not offered surgery if the attending physician believed that the patient would not survive an operative procedure or if it was believed that the patient would have no meaningful quality of life after surgery. The decision to palliate was taken in consultation with the patient and next of kin.

The following data items were extracted from the database: discharge status of patient (alive or dead), admission date and discharge date, age at admission, mode of admission and gender. Haemoglobin, white cell count, urea, sodium and potassium levels were used from the first set of blood taken on admission or those taken immediately pre-operatively. This was usually the sample taken on the day before or on the day of surgery. The cases were then ordered by dead/alive status at discharge (alive on discharge from hospital. Many patients remain on medical wards after amputation) and age at admission, and records were then placed alternately into 2 data sets. In-hospital mortality occurring later than 30 days after the operation was also included in this. Splitting the data like this ensured that there were equal numbers of deaths in both sets and that the age range was similar in each group. Using data from one as the training set, binary logistic regression (SPSS[®] version 11; SPSS, Chicago, Illinois, USA) was used to form a model of adverse clinical outcome (mortality at discharge).

The model was then applied prospectively to the second (validation) set of patients whose data had not been part of the original training set to develop the predictor equation. It is important to have adequate number of deaths in each set to model outcome using logistic regression. Typically, as a rule at least 10 outcome events per potential predictor variable are required to minimise the risk of a Type I error.⁹

Case notes were analysed retrospectively for observed in-hospital or ≤ 30 days of operation mortality.

Statistical Analysis

The overall performance of the model was assessed using techniques designed to test both calibration and discrimination.

The Hosmer–Lemeshow^{10–13} methodology was followed to assess the calibration of the model. This involves the use

of the chi-squared test to compare frequency tables obtained from prospective application of the equations. This is a null hypothesis test. A p value < 0.05 indicates a significant lack of fit. While it is possible to say that a model is wrong, i.e. did not predict outcome, it is not possible to state that a particular model is correct, only that it performed adequately.

The discriminative ability of the model was assessed using the c -index (equivalent to the area under the receiver-operator characteristic (ROC) curve. Discrimination is the ability of the model to appropriately rank patients in terms of risk – that is, the model's ability to ascribe high risks to high-risk patients and vice-versa. Values of 0.5 are no better than chance. It is generally accepted that reasonable models produce values in the range of 0.7–0.8 and good models give values 0.8–0.9.

The ability of the model to stratify risk was also demonstrated (Tables 1 and 2). Episodes were grouped within bands on the risk generated by the regression equation. The risk bands were chosen to give at least five predicted deaths in at least 80% of cases (Cochrane's rule) and to give, where possible, approximately equal predicted numbers in each risk range.

Results

We collected 579 records but had to exclude 41 (7%) due to incomplete documentation or lack of follow-up in the immediate post-operative period. Therefore the data used contained 538 complete records. The three hospitals contributed 281, 163, 94 cases, respectively, with the largest contribution from a tertiary referral teaching hospital. The other two hospitals were district general hospitals.

Binary logistic regression analysis of the laboratory and administrative data of the training set (Table 1) produced the following outcome model for lower limb amputations for critical ischaemia:

$$\ln_e\{R/(1-R)\} = 3.495 + (0.5942 \times \text{gender}) \\ + (1.069 \times \text{mode of admission}) \\ + (0.0119 \times \text{age on admission}) + (0.0319 \times \text{urea}\{\text{mmol/l}\}) \\ + (-0.0432 \times \text{sodium}\{\text{mmol/l}\}) + (-0.0037 \\ \times \text{potassium}\{\text{mmol/l}\}) + (-0.1260 \times \text{haemoglobin}\{\text{g/dl}\}) \\ + (0.0679 \times \text{white cell count}\{\times 10^9/l\}) + (-0.0004 \\ \times \text{creatinine}\{\mu\text{mol/l}\}) + (-3.397 \times (\text{urea}/\text{creatinine}))$$

R = the risk of death.

Gender takes the value 1 for male and 0 for female.

Mode of admission takes the value 0 for elective and 1 for non-elective admissions.

It was found that the model could successfully describe lower limb amputation mortality in the validation test set (Table 2). The equation also performed adequately in terms of discrimination.

Patient demographics are shown in Table 3.

Table 1 Mortality – model tested against training set

% Range predicted mortality	Number	Mean % predicted risk	Predicted deaths	Reported deaths	χ^2
0.0–20.9	72	12.99	9	10	0.05
20.9–28.2	35	25.62	9	10	0.16
28.2–32.3	31	30.02	9	11	0.44
32.3–36.2	27	34.10	9	5	2.92
36.2–40.3	27	38.77	10	7	1.88
40.3–44	17	41.90	7	7	0.00
44–48	15	45.52	7	8	0.37
48–50	16	48.98	8	10	1.17
50–58	17	53.59	9	11	0.84
58–100	12	64.79	8	7	0.22
0–100	269	31.96	86	86	8.05

$\chi^2 = 8.05$, 8 d.f., $p = 0.429$; no evidence of lack of fit; c -index = 0.704.

Discussion

The results of this study confirm that attempts at life-saving lower limb amputation for critical ischaemia are frustrated by a considerable rate of post-operative mortality (32%). We accept that our mortality rate is higher than in other series^{1,14,15} although the cohort of patients we used was selective and from several centres. It may also indicate that in some cases we were possibly too aggressive in our surgical approach when conservative or palliative strategies would have been more prudent. This calls for a better pre-operative quantitative stratification of the operative risk as well as identification of patients who may not benefit from surgical intervention.

This observational study focussed on the development and validation of a new VBHOM model addressing specifically post-operative mortality following lower extremity amputation for critical ischaemia. It was built from data

Table 2 Mortality – prospective application of the new VBHOM model to validation set

% Range predicted mortality	Number	Mean % predicted risk	Predicted deaths	Reported deaths	χ^2
0.0–20.1	77	12.11	9	11	0.34
20.1–27.5	39	24.02	9	8	0.26
27.5–32.9	31	30.20	9	15	4.87
32.9–37.7	27	35.02	9	9	0.03
37.7–41.4	21	39.29	8	6	1.01
41.4–45	18	42.95	8	9	0.37
45–49	17	46.64	8	8	0.00
49–55	15	51.72	8	4	3.77
55–64	14	59.70	8	9	0.12
64–100	10	72.72	7	6	0.82
0–100	269	31.53	85	85	11.60

$\chi^2 = 11.60$, 10 d.f., $p = 0.313$; no evidence of lack of fit; c -index = 0.677.

Table 3 Patient demographics of patients (*n* = 538)

Variable	Number
Number	538
Median age (years) (range)	75 (37–96)
Male (%)	309 (57)
Female (%)	229 (43)
Mean haemoglobin (\pm SD)	11.9 (\pm 1.1)
Mean white cell count (\pm SD)	10.9 (\pm 1.4)
Mean serum sodium (\pm SD)	135 (\pm 4.5)
Mean serum potassium (\pm SD)	4.5 (\pm 0.68)
Mean serum urea (\pm SD)	9.8 (\pm 5.8)
Emergency admission (%)	386 (72)
AKA:BKA:other	314:211:13
Observed in-hospital mortality (%)	171 (32)

collected retrospectively from three hospitals within the East Anglian region of the United Kingdom. As demonstrated, it provides a model that allows reasonable prediction (*c*-index = 0.6–0.7) of surgical mortality and validates previous work based on the VBHOM concept that the risk of in-hospital mortality can be modelled in patients undergoing index arterial operations such as AAA repair using a small number of commonly used laboratory and administrative items.^{6,8} One of the refinements made to this model is the addition of creatinine to the predictor equation. Previously urea was the only biochemical measure of renal function on the National Vascular Database (NVD) proforma. The use of creatinine clearance is likely to be a better indicator of renal impairment than urea alone.¹⁶

The ability to predict clinical outcomes from laboratory measurements taken from a single venesection pre-operatively would provide significant advantages. It could facilitate the optimal use of limited resources such as intensive care by allowing focussed surveillance of high-risk patients to be placed post-operatively in clinical areas capable of close monitoring and early therapeutic intervention. It may also allow the vascular surgeon to predict risk in an individual patient before surgery and this risk can be discussed confidently with both patient and relatives whilst gaining informed consent. If the predicted risk assessment is too high for a patient a less invasive procedure or conservative management may be entertained. Other advantages of this scoring system are that it is generally simple and applicable to all admissions and it is usually possible to collect all the items required as part of routine clinical care. Therefore it makes no demands on the staff providing the care and all that is necessary is access to the hospital information systems to view the results. The biochemical and haematological data items are precisely measurable, objective and are subject to the rigorous quality control processes implemented by the hospital laboratories. Furthermore the data required for predicting risk are likely to be available very soon after admission, irrespective of the mode of admission and the time of day.

The VBHOM approach was developed in response to the difficulty of collecting all data items required by the NVD on all patients in all centres submitting data to the NVD. It is essentially a minimalist approach designed to overcome the problem of missing data, which are the Achilles heel of all clinical data collection exercises.¹⁷ The VBHOM approach uses simple data that are possible to collect pre-operatively on all patients. It does not use any data collected at operation. All risk models can only predict risk within the “dimensions” of the data items used within the model. It is certain that there are numerous other factors, many of which would only be found at operation, which influence the risk of adverse outcome for individual patients. Besides co-morbidities, a multidisciplinary approach, referral pathway and revascularization policy have an important impact on the outcome of these patients^{18,19} but taking into consideration of these factors would lead to a complicated score, which would be difficult to use and implement universally. Furthermore cardiac disease is an important predictor of outcome but this is not used by VBHOM and despite this the model performs well. The haematological and biochemistry results may in fact be a surrogate marker for cardiac disease. For example, a high urea or low haemoglobin level may act as a surrogate marker for renal failure and cardiac disease, respectively.

This study did not include patients who were deemed unfit for amputation and were therefore palliated. The operative mortality is high but without surgery death was inevitable. It is often difficult to deny sick patients surgery if they understand death is the alternative. A prospective study would help to delineate this further.

Limitations of the study include the fact that retrospective data was used not only to generate but also to validate the model. Since 2006, lower extremity amputation has become one of the index arterial operations for which the Vascular Society of Great Britain and Ireland collects data on²⁰ and hence this new VBHOM model should not be taken as a definitive predictor equation. It will require refinement and is likely to evolve as knowledge increases and the NVD expands. It should be possible to validate the predictor equations generated in this study against data submitted to the NVD in the near future. However, although this approach may be generally applicable it should be further tested in other geographical locations before it is used to influence patient management.

Another limitation is that the data were collected from three hospitals. The baseline characteristics of the patients that were admitted may have been different, and it is possible that the model did not fully adjust for differences in these patient characteristics e.g. one hospital could treat mainly diabetics, the other patients in haemodialysis. Therefore, the training group and the validating group could be different by means of risk factors and the indications for amputation (CLI, embolism or Buerger's disease do not have the same risk). However, patients were assigned to the training and validation sets randomly and we have no reason to believe that the groups were different.

Conclusions

VBHOM provides a single unified model that allows reasonable prediction of surgical mortality after lower limb amputation for critical ischaemia. It may be useful to simplify comparative audit but will need greater refinement and validation before it can be used reliably for risk prediction in an individual patient before surgery.

Competing Interests

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