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Delay Influences Outcome after Lower Limb Major Amputation

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ABSTRACT

Aim: To investigate if a relationship exists between hospital waiting time to major amputation and outcome.
Method: All patients undergoing major lower limb amputation in England between April 2002 and March 2006 were identified from the Hospital Episodes Statistics (HES) data. Amputations related to trauma or malignancy were excluded.
The length of wait (LOW), from date of admission to date of major amputation was calculated. A two-level regression model was used to investigate if LOW had a significant effect on recovery time and in-hospital mortality.
Results were adjusted for age, sex, Charlson score, Social Deprivation, mode of intervention (bypass/angioplasty/no intervention) and mode of admission (emergency/elective).
Results: 14 168 major amputations were identified. 12 884 (90.9%) had no intervention prior to amputation on that admission.
Length of Wait (LOW) significantly prolonged recovery in men (Exponential Estimate 1.01 1.01–1.02 $p < 0.0001$) and women (EE 1.02 1.01–1.02 $p < 0.0001$) and increased in-hospital mortality in men (OR 1.02 1.02–1.03 $p < 0.0001$). Risk of in-hospital death increased by 2% for each day waited.
Conclusion: Delays in decision making or in getting a patient into the operating theatre have a negative effect on patient outcome in terms of overall length of stay and mortality after major lower limb amputation.

Introduction

Despite co-ordinated national efforts major lower limb amputation rates remain high worldwide[1] and carry with them significant in-hospital mortality ranging from 16.8% to 29.0%.[2,3] The rising global incidence of diabetes mellitus poses a considerable challenge to reducing amputation rates and although tackling this root cause is of paramount importance equal focus should be placed on reducing procedural mortality.

Delays in performing surgery has been demonstrated to have negative effects on outcome in some other acute surgical interventions, including small bowel obstruction[4] and fractured neck of femur.[5–7] Major lower limb amputation, like hemi-arthroplasty, is often the only treatment option available and although these patients tend to be elderly with significant co-morbidity, their operations are performed on emergency lists, out of hours and often by junior surgeons.

We have sought to establish if a relationship exists between the length of time a patient waits after admission to hospital prior to a major lower limb amputation and the subsequent outcome. Waiting time to surgery represents the time taken to attempt limb salvage or to make a decision that a limb is beyond salvage and primary amputation is required. In either case, these are challenging decisions based upon clinical judgement and experience with no independently validated risk scoring system to guide clinicians. Identifying factors that affect outcome after major lower limb amputation is vital to allow concerted efforts to be made to improve the processes and peri-operative care surrounding amputation to begin to drive down amputation related mortality.

Method

This study used the English National Health Service dataset, the Hospital Episode Statistics (HES). The HES were acquired for the years 2001–2006. Individual patient data were extracted relating to patients who underwent major lower limb amputation

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procedures between 2002 and 2006. The HES data contain information on every hospital admission in England at individual patient level amounting to more than 15 million records per year. An admission, or spell, is divided into a number of episodes with an episode being a period of care under one consultant. The data available are extensive and include patient level information on demographics, diagnostic and procedural coding and in-patient mortality. Individual patients are identified by a pseudonymised code (HESID) that allows an individual to be followed through the database, in time, across a number of hospital admissions to determine outcome. Diagnostic coding is recorded using the International Classification of Diseases version 10 (ICD-10) and procedures are coded with the Office of Population, Census and Surveys version 4 (OPCS-4) codes.

Outcomes

An in-house computer programme was developed that identified the 'index major amputation' which was defined as an above, through or below knee amputation of the lower extremity with corresponding OPCS-4 codes of X09, X10 and X11. Demographics, co-morbidities and previous operative procedures were identified and used to define co-morbid status using the Charlson co-morbidity score for each patient[8] which was used for risk adjustment. Attempted limb salvage by either arterial bypass, angioplasty or a combination of the two was recorded for each patient. Arterial bypass surgery could be an extra-anatomical, iliac, femoral or tibial bypass procedure as identified by corresponding OPCS-4 codes. Angioplasty could be iliac, femoral or tibial segment dilatation or stenting as identified their corresponding OPCS-4 codes. The length of wait (LOW) in days from admission to amputation was quantified as was the subsequent recovery time, in days, from date of surgery to discharge from hospital. The primary outcome measures were in-hospital mortality and post-procedural recovery time on the index admission.

Statistical analysis

A two level multivariate analysis and regression model was used to examine the effect of the multiple exposure variables on a binary outcome (in-hospital mortality) and a continuous outcome (length of recovery). These effects are reported as odds ratios (OR) with a 95% confidence interval (C.I.) from a logistic regression model for the binary outcome measure and as linear regression exponential estimates (EE) with 95% C.I. and *p*-value for the continuous outcome (length of recovery).

The following demographic, descriptive and co-morbidity variables were recorded for each patient and entered into the logistic regression model:

- Level of amputation (above, through or below the knee)
- Length of wait in days from admission to amputation
- Attempted limb salvage interventions performed on the index admission (angioplasty, arterial bypass or angioplasty and arterial bypass)
- Age
- Charlson score (made up of 14 disease categories with patients given a score of 0–3 with 3 conferring the greatest number of defined co-morbidities)[8]
- Mode of admission (emergency or elective)
- Social deprivation decile – a postcode based ranking of a patient's social deprivation based upon seven domains from the National Census 2001. Patients are ranked 1–32 482 from most deprived to least deprived.[9] This ranking has been divided into deciles for analysis.

Statistical analyses were performed using SAS version 9.1 running the PROC GLIMMIX procedure (SAS Institute, Cary, North Carolina, USA).

Results

A total of 14 168 major lower limb amputations were identified over the 5 year time period. 9336 (65.9%) were male patients and the mean age was 70 years. Summary demographics are shown in Table 1. 6940 (49.0%) patients underwent above knee amputations, 6934 (49.0%) below knee and 404 (2%) through the knee amputations giving a National above knee to below knee ratio of 1:1. On the index admission 12 884 (90.9%) of patients had no attempt at revascularisation (bypass or angioplasty) but may have had attempted revascularisation on previous admissions. 504 (3.6%) had an arterial bypass procedure prior to amputation in the index admission, and 700 (4.9%) patients had a preceding angioplasty attempt. 80 (0.56%) had both angioplasty and arterial bypass on the index admission. Only 12.7% of patients were coded as having gangrene or tissue loss despite 75.2% (10 591) being emergency admissions. On initial analysis the differences in outcome between male and females was so disparate that they were separated into individual cohorts for the purposes of statistical analysis. These results are summarised in Table 2 with males and females analysed separately.

Table 1
Descriptive statistics of 14 168 patients identified who underwent major lower limb amputation. Results are divided into groups according to attempted revascularisation on the index amputation admission. *P*-values are results of Chi–Square test examining difference between proportions in each of the intervention groups.

	Overall	No intervention	Angioplasty	Arterial bypass	Angioplasty and bypass	*P*-value
Number of patients	14168	12884 (90.9%)	700 (4.9%)	504 (3.6%)	80 (0.6%)	<0.0001
Above knee amputation	6940 (49.0%)	6446 (92.9%)	212 (3.1%)	258 (3.7%)	24 (0.3%)	<0.0001
Through knee amputation	404 (2.0%)	385 (95.3%)	14 (3.5%)	5 (1.2%)	0	<0.0001
Below knee amputation	6937 (49.0%)	6371 (91.8%)	336 (4.8%)	207 (3.0%)	23 (0.3%)	<0.0001
Age	70	70	71	70	70	$p > 0.05$
Male gender	9336 (65.9%)	8630 (92.4%)	359 (3.8%)	314 (3.4%)	33 (0.4%)	<0.0001
Diabetes mellitus	6197 (43.7%)	5723 (92.4%)	308 (5.0%)	138 (2.2%)	28 (0.5%)	<0.0001
Chronic kidney disease	1496 (11.0%)	1375 (92.0%)	87 (5.8%)	29 (1.9%)	5 (0.3%)	0.0013
Gangrene or tissue loss	1795 (12.7%)	1521 (84.7%)	154 (8.6%)	103 (5.7%)	17 (0.9%)	<0.0001
Elective admission	3577 (25.2%)	3342 (90.6%)	112 (3.1%)	105 (2.9%)	18 (0.5%)	<0.0001
In-hospital mortality (Crude)	2403 (17.0%)	2140 (89.0%)	128 (5.3%)	113 (4.7%)	22 (0.9%)	0.0026
One year mortality (Crude)	5012 (35.4%)	4537 (90.5%)	261 (5.2%)	180 (3.6%)	34 (0.7%)	0.5119
Median Charlson score	2	2	2	2	2	–
Median deprivation rank	13611	13277	12200	13952	12002	0.5165
Median total length of stay (days)	33	26	35	35	34	<0.0001
Median post amputation recovery time (days)	22	19	22	24	24	<0.0001

Overall there was a crude unadjusted in-hospital mortality rate of 17.0% rising to 35.4% at one year. Median total length of stay was 33 days with a median of 22 days spent recovering from major amputation. In the no intervention group a median of 7 days was spent waiting from admission to amputation.

Waiting time and in-hospital mortality

There were significant differences in outcomes seen between different hospital trusts for men and women (Table 2). Length of wait to amputation had a significantly detrimental effect on male in-hospital mortality ($p < 0.0001$ OR 1.02 1.02–1.03) with each extra day waited increasing the risk of mortality by 2%. It did not reach significance in the female cohort ($p = 0.1216$ OR 1.01 1–1.02). These data are represented in Fig. 1 which shows predicted in-hospital mortality curves modelled on a 70 year old man and woman with the median Charlson co-morbidity score. This demonstrates the relationship between increased waiting time and mortality after major lower limb amputation.

Waiting time and length of recovery

There were significant differences in outcomes seen between different hospital trusts for men and women (Table 3). Increasing length of wait to amputation significantly increased recovery time in both male and female patients after major lower limb amputation ($p < 0.0001$ EE 1.01 1.01–1.02 and $p < 0.0001$ EE 1.02 1.01–1.02 respectively). These data are represented in Fig. 2. This graph uses recovery curves modelled on a 70 year old man and woman with the median Charlson co-morbidity score to demonstrate the relationship between increasing wait to surgery and increased recovery time.

Intervention and mortality

12 884 (90.9%) of patients had no form of attempted limb salvage intervention (angioplasty or bypass) on their index admission before undergoing major amputation. Crude in hospital mortality rates shown in Table 1 show a higher mortality in patients who underwent attempted revascularisation (28% in angioplasty and bypass group vs. 17% in the no intervention group $p < 0.0001$) and this carried through into the adjusted regression modelled data. Attempted limb salvage by arterial bypass increased in-hospital mortality in men (OR 1.50 95% C.I. 1.12–2.0 $p = 0.006$) and women (OR 1.63 95% C.I. 1.11–2.38 $p = 0.012$) compared to no intervention. Angioplasty in either men or women failed to have a significant effect on mortality but a combination of attempted angioplasty and arterial bypass increased in-hospital mortality by OR 2.35 (1.26–4.39 $p = 0.008$). These results are depicted in Fig. 3 which shows predicted mortality curves derived from the regression model based upon a male aged 70 years old with a median

Table 2
Results of two level multivariate logistic regression model examining effects of defined variables on in-hospital mortality after major lower limb amputation. Interventions refer to the index admission and are compared to 'no intervention' as baseline. 'No intervention' does not include prior attempts at revascularisation on previous admissions. Variables significantly increasing in hospital mortality are shaded red, those significantly reducing mortality are shaded green.

Variable	p-value	Odds Ratio	95% Confidence Interval	p-value	Odds Ratio	95% Confidence Interval
	Female			Male		
Variance between Hospitals	<0.0001	-	-	<0.0001	-	-
Above knee Amputation	<.0001	1.52	1.28-1.8	<.0001	1.48	1.3-1.68
Length of Wait to Amputation	0.164	1.01per day	1-1.02	<.0001	1.02 per day	1.02-1.03
No Intervention	-	1.0	-	-	1.0	-
Angioplasty	0.340	0.84	0.58-1.20	0.216	1.18	0.91-1.52
Arterial Bypass	0.012	1.63	1.11-2.38	0.006	1.50	1.12-2.0
Angioplasty and Bypass	0.782	1.15	0.42-3.17	0.008	2.35	1.26-4.39
Age	<.0001	1.03	1.02-1.04	<.0001	1.04	1.03-1.04
Charlson Co-morbidity Score	<.0001	1.66	1.49-1.84	<.0001	1.72	1.58-1.87
Elective Admission	<.0001	0.38	0.3-0.48	<.0001	0.53	0.45-0.63
Diabetes Mellitus	<.0001	0.58	0.49-0.70	<.0001	0.55	0.48-0.63
Chronic Kidney Disease	0.0019	1.52	1.17-1.98	<.0001	1.51	1.27-1.8
Social Deprivation Decile	0.740	1	0.97-1.02	0.2424	0.99	0.96-1.01

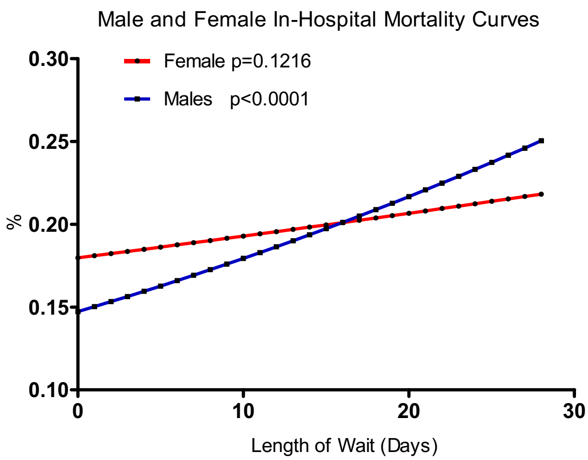

Figure 1. In-hospital mortality curves post major amputation plotted using predicted data from a 2 level regression model of a 70 year old male and female with median Charlson score undergoing no attempt at revascularisation on the index admission. The graph demonstrates the relationship between length of wait to surgery and increased mortality after major lower limb amputation.

Charlson co-morbidity score (2) and demonstrate the relationship between intervention and probability of in-hospital death.

Intervention and recovery

Attempted limb salvage by angioplasty, arterial bypass or a combination of the two significantly extends a patient's recovery time after major amputation compared to no attempt at revascularisation prior to amputation. These results are summarised in Table 3.

Discussion

Major lower limb amputation and its associated mortality remain a significant burden to health systems and patients worldwide despite concerted efforts to tackle the problem. Actions to address the rising incidence of diabetes mellitus and the associated diabetic foot syndrome have been introduced and meetings dedicated to lower limb salvage have gained popularity.[10] While these seek to tackle the root cause of the majority of lower limb major amputations very little data are available on the effects of hospital processes and administration on the outcomes of those patients whose pathology is already too advanced to benefit from prevention and in whom amputation is inevitable.

The data presented here are derived from National data over a 5 year period and have typical demographic characteristics of patients routinely seen on vascular surgical units around the United Kingdom and is comparable to previously published studies.[11–13] The population is largely male (66%), elderly (median age 70) with a high proportion of Diabetes Mellitus (43.7%) and Chronic Kidney Disease (11.0%). These figures support the validity and applicability of this data and are supported by recent studies demonstrating the validity of HES data.[14] The relatively low proportion of patients coded as having tissue loss or gangrene (12.7%) represents poor clinical coding rather than a reflection of

Table 3
Results of two level multivariate regression model examining effects of defined variables on length of patient recovery after major lower limb amputation. Interventions refer to the index admission and are compared to 'no intervention' as baseline. 'No intervention' does not include prior attempts at revascularisation on previous admissions. Variables significantly increasing the length of patient recovery are shaded red, those significantly shortening recovery are shaded green.

Variable	p-value	Exponential Estimate	95% Confidence Interval	p-value	Exponential Estimate	95% Confidence Interval
	Female			Male		
Variance Between Hospitals	Yes <.0001	-	-	Yes <.0001	-	-
Above knee Amputation	0.323	0.97	0.92 – 1.03	0.0177	0.95	0.92 – 0.99
Length of Wait to Amputation	<.0001	1.02 per day	1.01 – 1.02	<.0001	1.01per day	1.01 – 1.02
No Intervention	-	1.0	-	-	1.0	-
Angioplasty	0.984	1.0	0.89-1.12	0.001	1.12	1.01-1.23
Arterial Bypass	0.036	1.17	1.01-1.36	0.027	1.12	1.01-1.23
Angioplasty and Bypass	0.013	1.56	1.10-2.22	0.672	1.06	0.82-1.37
Age	<.0001	1.01	1 – 1.01	<.0001	1.01	1.01 – 1.010
Charlson Co-morbidity Score	0.181	1.02	0.99 – 1.06	0.002	1.04	1.02 – 1.07
Elective Admission	<.0001	0.85	0.81 – 0.91	<.0001	0.84	0.80 – 0.87
Diabetes Mellitus	<.0001	1.14	1.07 – 1.21	0.147	1.03	0.99 – 1.08
Chronic Kidney Disease	0.886	1.01	0.91 – 1.12	0.238	1.04	0.98 – 1.11
Social Deprivation Decile	<.0001	0.98	0.97 – 0.99	0.001	0.99	0.98 – 0.99

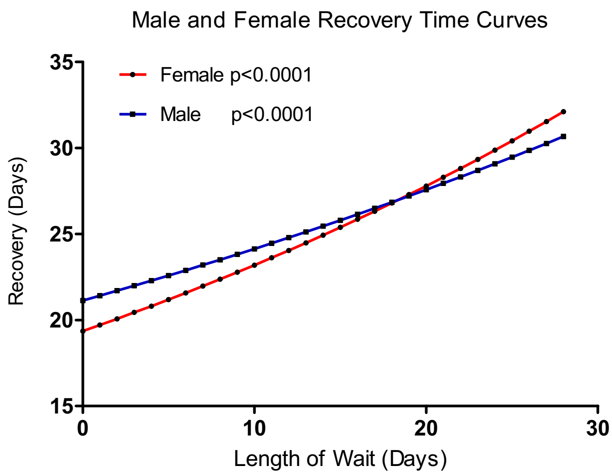

Figure 2. Recovery time post major amputation curves plotted using predicted data from a 2 level regression model of a 70 year old male and female with median Charlson score undergoing no attempt at revascularisation on the index admission. The graph demonstrates the relationship between length of wait and increased recovery time after major lower limb amputation.

actual presenting complaint with this particular data only being present in the HES data in 40% of cases.

Median length of hospital stay in these patients is high and likely reflects the degree of co-morbidities present on admission and the complexity in arranging discharge from a social services perspective at the end of their stay but is comparable to previously published data.[15] We did not report data on the use of managed care so are unable to draw conclusions regarding the proportion of patients requiring increased social care on discharge compared to admission. It was interesting that increased social deprivation prolonged the postoperative length of recovery, reflecting the increased difficulty of arranging social care (and the consequent delays in discharge) for those with more limited means of self funded care or from more deprived areas with less well established social services.

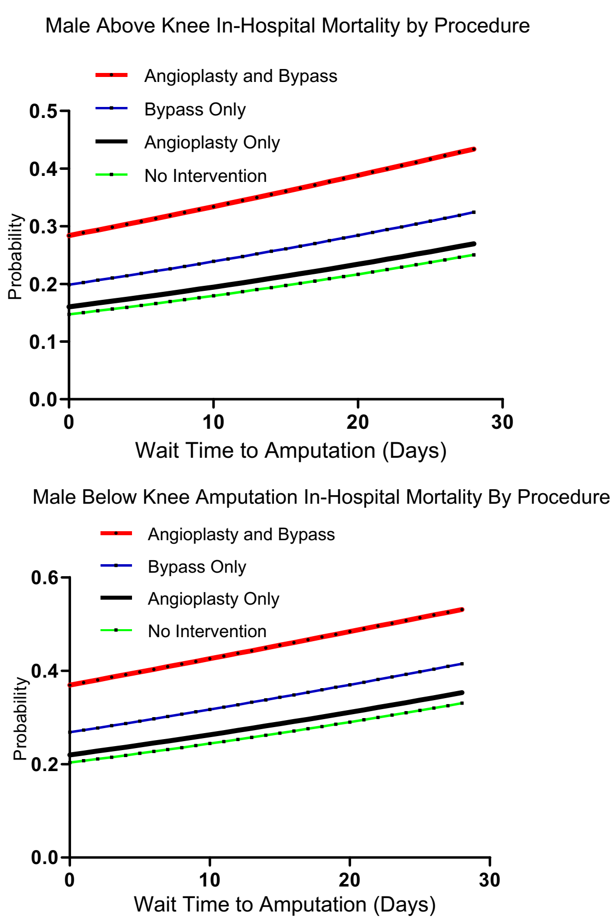

Figure 3. Predicted mortality curves over time of a 70 year old male undergoing above and below knee amputation with median Charlson co-morbidity score of 2 comparing the effects of attempted revascularisation on the index admission against probability of in-hospital death.

A direct and significant relationship has been demonstrated between the length of time a patient waits for a major amputation and their mortality and recovery time with the risk of in-hospital death increasing by 2% and length of recovery increasing by one day for each day waited. Such a relationship demonstrates that changes to the administrative and service pathways in hospitals could potentially improve a patient's outcome and reduce costs if they undergo their operation sooner. This is further supported by the median length of wait from admission to major amputation in all patients of eleven days and in particular a median wait of seven days when no attempt at revascularisation is made. Although some of this time will be set aside for diagnostics and medical optimisation it would seem likely that improvements could be made in particular to decision making and theatre time utilisation with corresponding effects on mortality. It is a limitation of the study that the precise time the decision to amputate is taken cannot be established from the HES but it is likely that the majority of the median wait of 7–11 days is post decision to amputate. A recently published study on delay and mortality after repair of hip fractures suggests a delay of 120 h because of co-morbidities is acceptable but beyond this becomes a significant risk[16]and a similar figure maybe appropriate for lower limb amputation. Although we have shown a significant relationship between waiting time to surgery and outcome (mortality and recovery time) for major lower limb amputation these effects are small in comparison with the other variables tested in the model. As can be seen in Tables 2 and 3 chronic kidney disease, increasing Charlson co-morbidity score and above knee amputation to name a few have significantly larger effects on outcome than delay to surgery (OR 1.52, 1.66 and 1.52 respectively for mortality). While the effect of delay is more modest it is, none the less, significant and illustrates that a multi-faceted approach to improving the care of prospective amputees is needed to drive down mortality.

On the whole the effects of the variables examined are similar in men and women but in the key variable of Length of Wait to surgery men and women differ considerably. It is the relatively small effect of delay that likely accounts for the lack of statistical significance in mortality in women seen in the results rather than female sex itself being protective.

Previous work has demonstrated that 56.7% of patients who underwent major lower limb amputation in England between 2003 and 2008 had no attempt at revascularisation in the two years prior to amputation.[2] This supports our finding that a very high proportion of patients (90.9%) have no attempt at limb salvage on the index admission and has to be a focus of improvement in the future. This figure reflects the poor condition that the majority of lower limbs present in that render them unsalvageable with the only treatment options palliation or primary amputation. This could be a consequence of failure of detection in primary care, poor patient education and the rapidity with which critical ischaemia and gangrene can develop or most likely, a combination of all three.

Although not designed to measure the effect of revascularisation on amputation rates this study has demonstrated a negative relationship between attempted revascularisation before amputation compared with no intervention at all on mortality and length of recovery. The reasonably small numbers of patients who underwent attempted (albeit failed) limb salvage had a higher odds ratio of in-hospital mortality and will be the group of patients who presented with a potentially salvageable limb. Changes in practice that lead to early detection of potential ischaemia and early referral to a vascular specialist for consideration of revascularisation may have a significant effect on major amputation rates and its associated mortality but the additive effect of failed intervention before major amputation should always be considered. This combined with changes in service delivery to ensure those that do require a major amputation are operated on promptly will go a long way to tackling the burden of amputation.

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Conflict of interest

None.

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