Are systemic emboli reduced in computer-assisted knee surgery?

A PROSPECTIVE, RANDOMISED, CLINICAL TRIAL


From SPORTSMED SA, Adelaide, South Australia

We undertook a prospective, randomised study using a non-invasive transcranial Doppler device to evaluate cranial embolisation in computer-assisted navigated total knee arthroplasty (n = 14) and compared this with a standard conventional surgical technique using intramedullary alignment guides (n = 10). All patients were selected randomly without the knowledge of the patient, anaesthetists (before the onset of the procedure) and ward staff. The operations were performed by a single surgeon at one hospital using a uniform surgical approach, instrumentation, technique and release sequence. The only variable in the two groups of patients was the use of single tracker pins of the imageless navigation system in the tibia and femur of the navigated group and intramedullary femoral and tibial alignment jigs in the non-navigated group.

Acetabular Doppler signals were obtained in 14 patients in the computer-assisted group and nine (90%) in the conventional group, in whom high-intensity signals were detected in seven computer-assisted patients (50%) and in all of the non-navigated patients.

In the computer-assisted group no patient had more than two detectable emboli, with a mean of 0.64 ($\pm$ 0.74). In the non-navigated group the number of emboli ranged from one to 43 and six patients had more than two detectable emboli, with a mean of 10.7 ($\pm$ 13.5). The difference between the two groups was highly significant using the Wilcoxon non-parametric test ($p = 0.0003$).

Our findings show that computer-assisted total knee arthroplasty, when compared with conventional jig-based surgery, significantly reduces systemic emboli as detected by transcranial Doppler ultrasonography.

Total knee arthroplasty (TKA) may cause paradoxical embolism producing complications such as confusion, respiratory impairment, deep-vein thrombosis, ileus, renal impairment, pancreatitis and occasionally fat embolism.1-4

Computer navigation has been developed to allow accurate intra-operative positioning of the components without breeching the intramedullary cavities.5 This may decrease the incidence of systemic embolisation. It is thought that these emboli occur secondary to elevated intramedullary pressures generated by intramedullary alignment rods.6,7 Lengthened operating times, as currently occur in computer-assisted surgery, and other undetermined factors may, however, negate this benefit.

We undertook a prospective, randomised study using a non-invasive transcranial Doppler device to evaluate cranial embolisation in computer-assisted navigated TKA and compared this with the conventional surgical technique using intramedullary alignment guides. In laboratory models selected high-intensity transient signals detected by transcranial Doppler ultrasonography have been shown to correspond to micro-emboli composed of either air, platelets, fibrinogen, fat or atheromatous material.5,9 They have also been detected in various clinical settings.10-16

Cerebral micro-embolism occurs frequently during surgical procedures, even in the absence of a patent foramen ovale. The passage is believed to be through the pulmonary capillaries or shunting through recruitable pulmonary vessels.17

Large embolic loads have been associated with cognitive impairment, pulmonary complications and increased mortality.18-20 Detected cranial emboli have also been shown to correlate with transoesophageal echocardiographic findings, allowing observation of emboli without the invasive monitoring associated with it.21 Furthermore, these findings, have been correlated with MRI observations.22

The use of ultrasound to detect emboli is not new in orthopaedic surgery.23
Our primary outcome measure was the detection of the number of micro-emboli and the secondary outcome measure was the alteration in the mental test score and standard post-operative monitoring of temperature, and cardiac and respiratory parameters on days one and three after operation.

Patients and Methods

We excluded patients with a history of stenosis of the carotid artery and those with a likely source of arterial emboli such as atrial fibrillation or a prosthetic valve. The remaining patients who were undergoing a unilateral TKA for osteoarthritis were selected randomly by the toss of a coin without the knowledge of the patient, anaesthetist (before the onset of the procedure) and ward staff (who conducted the mental test scores). Approval of the ethical committee had been granted and all patients gave informed consent. Patients were advised to discontinue non-steroidal anti-inflammatory medication, one week before surgery. The procedures were performed by a single surgeon (AJS) at one institution in a standardised manner. A bloodless field was obtained by the use of a pneumatic tourniquet at a pressure of 350 mmHg; a standardised manner. A bloodless field was obtained by the use of a pneumatic tourniquet at a pressure of 350 mmHg. The intramedullary guides were inserted into the tibia and femur in the navigated group. No attempt was made to perform minimally-invasive surgery.

When using the intramedullary guides all attempts were made to reduce marrow embolisation. The intramedullary entry holes were overdrilled to exceed the diameter of the alignment rod in order to allow marrow contents to bypass the rod and to decrease intramedullary pressure. The rods were introduced slowly and were fluted to assist the egress of marrow elements in order to reduce further the intramedullary pressure and the likelihood of pulmonary shunting.

All patients had a unilateral primary TKA using an uncemented hydroxyapatite-coated press-fit Scorpio knee (Stryker Howmedica Osteonics Corp., Allendale, New Jersey) with a cemented patellar button.

All patients had spinal or general anaesthesia and femoral nerve block from one of two anaesthetists (RC, PD). Transcranial Doppler technique. Monitoring was carried out on all patients using a MultiDop X system (Multi-Dop X2; DWL Elektronische Systeme GmBH, Hamburg, Germany) with automatic software for detecting emboli intra-operatively, monitoring blood flow continuously and quantifying the occurrence and distribution of cerebral micro-emboli. This device traces the moving embolus at two different depths in the same artery and takes the time delay of its appearance as the crucial criterion. The system uses a 128 Fast Fourier Transform with 60% overlapping and Blackman man time-weighted function. The sample volume (gate) was set at 10 mm. The power was set at 0.6 mW for the duration of monitoring. Signals were obtained from the left middle cerebral artery in all patients. A headband secured a 2 MHz probe to the temporal region, anterior to the ear and superior to the zygomatic arch. The middle cerebral artery was localised by both auditory and visual signals to obtain the best signal/blood flow. Depth settings were between 46 and 54 mm in order to optimise the signal. All micro-emboli registering above 12 dB were counted. Preliminary studies on patients undergoing arthroscopy or even non-surgical manoeuvres in sedated or anaesthetised patients and the use of diathermy showed signal artefacts below this level. Other studies have also used this as a cut-off and have suggested a higher level to be more specific. Micro-emboli counts were recorded from the time of the application of the tourniquet until ten minutes after it had been released since no emboli were detected five minutes after release. The timing of any major procedural event was recorded such as the introduction of femoral and tibial rods, bone preparation, the introduction of trial components and the definitive prosthesis and release of the tourniquet.

### Table I. Details (mean ± SD; range) of the 24 patients

<table>
<thead>
<tr>
<th></th>
<th>Computer-assisted group (n = 10)</th>
<th>Non-navigated group (n = 14)</th>
<th>p value</th>
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<tbody>
<tr>
<td>Age (yrs)</td>
<td>64 ± 9.9 (48 to 81)</td>
<td>63 ± 10.0 (45 to 78)</td>
<td>0.86</td>
</tr>
<tr>
<td>Female (%)</td>
<td>35.7</td>
<td>70</td>
<td>0.61</td>
</tr>
<tr>
<td>Mean weight (kg)</td>
<td>94.8 ± 17.6 (65 to 130)</td>
<td>91.7 ± 12.6 (70 to 114)</td>
<td>0.64</td>
</tr>
<tr>
<td>% with ASA grade I or II</td>
<td>100</td>
<td>100</td>
<td>N/A*</td>
</tr>
<tr>
<td>Patients receiving spinal anaesthesia (%)</td>
<td>71.4</td>
<td>70</td>
<td>N/A</td>
</tr>
<tr>
<td>Pre-operative Hb (g/dl)</td>
<td>134.9 ± 15.9 (72 to 105)</td>
<td>136.3 ± 12.4 (113 to 154)</td>
<td>0.81</td>
</tr>
<tr>
<td>Tourniquet time (mins)</td>
<td>86.8 ± 10.2 (72 to 105)</td>
<td>73.4 ± 11.8 (62 to 95)</td>
<td>0.001</td>
</tr>
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* ASA, American Society of Anaesthesiologists
† N/A, not available
Statistical analysis. In the absence of any significant previous data to aid calculation of sample size, it was decided to start the study and to use the first two patients in each group for the estimation.

Sample size estimations were carried out with alpha and beta set at 5% and 20%, respectively. It was thought that a clinically significant reduction in emboli would be 50% (i.e. 15). Research in the literature suggested an SD of 11 in TKA. The required sample size per group was thus determined to be nine (n = 15.7 x σ²/δ²). Review of the literature also suggested that only 40% to 70% of patients have intra-operative cranial embolisation and in some patients there may be technical difficulties in obtaining an adequate Doppler signal. Thus, this figure of nine was increased to a minimum of ten in each group to allow for any difficulties that might occur.

Statistical analysis was performed using the R package (http://www.R-project.org) and Microsoft Excel for Windows. The statistical analysis was based on two independent groups of patients (computer-assisted, n = 10; control (non-navigated), n = 14). A t-test for assumption of no differences between the two baseline groups was carried out for age and weight. For categorical variables such as gender, co-morbidities (ASA) and anaesthesia, a z-test was used.

The numerical variables were found to be highly skewed and the Wilcoxon test was used for all comparisons. All p values were two-tailed, with p ≤ 0.05 considered to indicate statistical significance. A Bonferroni adjustment was also applied to allow for multiple testing. The relationship between the number of emboli detected and variables such as the mental test score and saturation were explored using regression statistics.

Results
There was a significantly longer mean tourniquet time (13.4 minutes) in the computer-assisted group which is consistent with the use of navigation.

Acceptable Doppler signals were obtained in all patients in the computer-assisted group and nine (90%) in the non-navigated group. In the patients with acceptable Doppler signals, high-intensity transient signals were detected in seven of the computer-assisted patients (50%) and all of the non-navigated patients.

In the computer-assisted group no patients had more than two detectable emboli, with a mean of 0.64 (SD 0.74). In the non-navigated group the number of emboli ranged from one to 43 and six patients had more than two detectable emboli with a mean of 10.7 (SD 13.5). The difference between the two groups was highly significant (p = 0.0003). The distribution of the emboli as a percentage of patients in the two groups is shown in Figure 1.

Almost all the emboli occurred at the time or soon after rodding of the femur in the non-navigated group and at the time of insertion of the trial prosthesis in the computer-assisted group.

The mean mental test score on day one was 7.9 in the computer-assisted group and 8.9 in the non-navigated group. However, this difference was not statistically significant (p = 0.29). On day 3 it was less, 9.4 in the computer-assisted group and 9.3 in the non-navigated group. Similar comparisons were made for pulse, blood pressure, oxygen saturation and temperature in the two groups on days one and three after surgery (Table II). None of these comparisons produced a significant difference.

To allow for multiple testing, a Bonferroni adjustment was applied to all 15 comparisons. This did not change the conclusion, namely that there was a significant reduction in the numbers of detectable emboli, but no other significant changes.

Regression statistics confirmed the presence of a negative coefficient when emboli were plotted against all the variables considered. However, the p values for all of these comparisons were not significant. The relationship between the mental test score on day one and emboli (along with the regression equation) is shown in Figure 2.

Discussion
Our findings show that there was a highly significant reduction in the number of cranial emboli as detected by automated transcranial Doppler ultrasonography in the computer-assisted group when compared with the non-navigated group.

Unfortunately, the transcranial Doppler ultrasonography used did not determine the nature of the emboli i.e. air, platelets, bone or fat, nor did it provide a definitive idea as to the size of the emboli.

The emboli detected in conventional surgery occurred at the time of or soon after the passage of the femoral alignment rod suggesting that the use of intramedullary rods...
contributes to the creation of systemic emboli. This is supported by other studies in TKA in which intramedullary guides have been implicated as the major factor that produces fat embolism by elevating the intramedullary pressure.\(^6,7\) Similar findings have been reported in hip arthroplasty.\(^35\) Other studies have also shown that cerebral micro-embolism occurs frequently during surgical procedures, even in the absence of a patent foramen ovale. This passage is believed to occur through the pulmonary capillaries or the opening of recruitable pulmonary vessels, i.e. a transpulmonary route.\(^36\)

The occasional emboli noted in the computer-assisted knees occurred during the insertion of the prosthesis and may have been caused by a transient elevation of intramedullary pressure at this time.

We used uncemented components and it has been documented that the use of cement is associated with much larger systemic embolic loads.\(^24,37-39\)

The number of emboli detected systemically in the middle cerebral artery is only an indication of the emboli released by the surgery. A much larger quantity is likely to have been deposited into the lung vasculature and to affect oxygenation.\(^27\) The elevation of the right arterial pressure because of pulmonary embolisation has been postulated to increase shunting across a patent foramen ovale which may have been otherwise not clinically evident\(^40\) and thus increase the amount of emboli released into the left-side systemic circulation as detected by transcranial Doppler ultrasonography.

A review of the literature suggested that certain groups of patients may be more at risk of systemic embolisation, such as in the presence of a large and spontaneous patent foramen ovale and with bilateral arthroplasty.\(^1,6,17,35,37\) The benefits of navigation surgery in terms of systemic effects such as confusion may be more pronounced in these high-risk groups of patients.

This is the first study to show that computer-assisted knee surgery, when compared with conventional surgery with femoral intramedullary alignment rods significantly reduces the number of systemic cranial emboli as detected by transcranial Doppler ultrasonography. However, our study did not show any statistical significance with regard to our secondary outcome measures. We estimate from this study that to show significance in the difference of the mental test score on day one an excess of 60 patients in each group would be required.

<table>
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<th>Table II. Secondary outcome measures in both groups</th>
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<tr>
<td>Variables</td>
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<tr>
<td>Mental test score</td>
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<td>Day 1</td>
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<td>Day 3</td>
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<td>Respiratory rate</td>
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<td>Oxygen saturation</td>
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<td>Day 1</td>
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<td>Day 3</td>
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<td>Pulse rate</td>
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<td>Day 1</td>
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<td>Day 3</td>
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<td>Blood pressure (mmHg)</td>
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<td>Systolic</td>
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<tr>
<td>Diastolic</td>
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<td>Temperature (°C)</td>
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<td>Day 1</td>
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<tr>
<td>Day 3</td>
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The authors wish to thank: Ms Susannah Lock and Dr Gary Glonek of AdStat for their assistance with statistics; our anaesthetists Roy Chesters and Prem Dhillon for assistance with monitoring; Rebecca McCarten (research nurse) for the collection of the data and Andrew Giles for assistance with the navigation equipment.

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References