ORIGINAL ARTICLE

Total arterial revascularisation as a primary strategy for coronary artery bypass grafting

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Background: Bilateral internal thoracic arteries confer improved survival benefit after coronary artery bypass grafting (CABG). Despite increasing evidence, the use of arterial conduits has not been accepted as a primary practice in most of the centres in the UK for various reasons. A series of patients has been analysed to assess the feasibility of total arterial revascularisation as a primary strategy in patients requiring first time CABG.

Methods: Altogether 245 patients undergoing first time CABG by one surgeon, from June 1999 to October 2000, were studied. Group 1 consisted of 165 patients undergoing total arterial revascularisation (using bilateral internal thoracic and radial arteries) and group 2 consisted of 80 patients undergoing conventional CABG (using one internal thoracic artery and supplemental veins). Thirty day mortality and early morbidity with particular reference to resternotomy for bleeding, cerebrovascular accidents, renal failure, and sternal dehiscence were the main outcome measures.

Results: Patients in group 1 were younger (mean (SD) 60 (10) *v* 65 (9) years; p<0.001), had lower Parsonnet scores (mean (SD) 5 (5) *v* 11 (7); p<0.001), and better left ventricular function. Both groups received a similar number of grafts. The percentage of patients undergoing total arterial revascularisation rose from 44% in the first three months to over 75% in the three latter three month periods. Overall 30 day mortality was 1.3%, one patient (0.6%) in group 1 and two patients (2.5%) in group 2. There was a similar incidence of postoperative complications and length of median postoperative stay in both groups.

Conclusion: Total arterial revascularisation can be adopted as a primary strategy in most patients undergoing CABG with no increase in mortality or morbidity.

The clinical and prognostic benefits of coronary artery bypass grafting (CABG) for certain anatomical patterns of coronary artery disease are well accepted.[1] Most patients undergoing CABG require three or four bypass grafts and the "standard" operation uses a single internal thoracic artery (ITA) to the left anterior descending coronary artery,[2 3] and supplemental vein grafts to the other coronary vessels.

The excellent early results of CABG are limited in the long term by vein graft failure. Ten years after CABG three quarters of vein conduits are blocked or severely diseased,[4] whereas more than 90% of ITA grafts are patent and disease free. Vein graft failure leads to reduced survival, recurrent angina, late myocardial infarction, and the need for further intervention,[5] so that by 10–15 years after the initial operation up to 40% of patients may require redo CABG at increased risk and cost.[6–8] Aspirin and lipid lowering agents improve vein graft patency rates over the medium term,[9 10] but it is not known if they will significantly improve long term patency rates.

The use of the left ITA to the left anterior descending coronary artery is the most important factor for survival and reduction of late cardiac events after CABG.[1–3] The limited life expectancy of vein grafts makes the rationale of total arterial revascularisation theoretically persuasive but fewer than 10% of the patients undergoing CABG in the UK receive two or more arterial grafts.[11] The two main reasons cited against arterial revascularisation are inadequate evidence of benefit and that it increases perioperative mortality and/or morbidity. While there have been no randomised trials of total arterial revascularisation compared with conventional surgery, several large studies have recently reported that multiple ITA grafts offer survival advantages over a single ITA graft.[8 12–16] In a recent meta-analysis of almost 16 000 patients comprising 11 269 single and 4693 bilateral ITA patients matched for age, gender, left ventricular function, and diabetes the bilateral ITA group had significantly better survival (hazard ratio for death 0.81, 95% confidence interval 0.70 to 0.94).[17] Furthermore, the perception that arterial revascularisation contributes to increased perioperative mortality and morbidity is not supported by current literature.

After publication of the Cleveland Clinic report of substantial clinical and survival benefits of bilateral ITA grafting in May 1999[8] we started total arterial revascularisation, using both ITA and the radial artery, as our primary strategy in all patients undergoing first time CABG. We assess the feasibility of this approach and present our early experience with particular reference to mortality and morbidity.

METHODS

The study includes all 245 patients undergoing first time CABG by one surgeon (DPT) from 1 June 1999 to 30 October 2000, since adopting a strategy of total arterial revascularisation.

Of these patients, 165 (67%) underwent total arterial revascularisation (group 1) and 80 (33%) had conventional CABG (group 2). All patients were assessed at a follow up clinic at six weeks. In particular, mortality at 30 days and postoperative complications including excessive bleeding requiring reoperation, cerebrovascular accidents, impairment of renal function, and sternal wound breakdown were assessed.

Abbreviations: ACE, angiotensin converting enzyme; CABG, coronary artery bypass grafting; ITA, internal thoracic artery

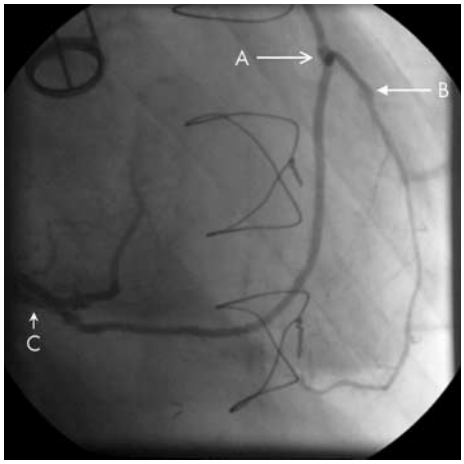

Figure 1 Angiogram showing right ITA to left anterior descending coronary artery, with a composite radial artery graft to the distal circumflex coronary artery in a patient with previous aortic valve replacement. A, radial artery from right ITA (composite graft); B, right ITA to left anterior descending coronary artery; C, radial artery to distal circumflex coronary artery.

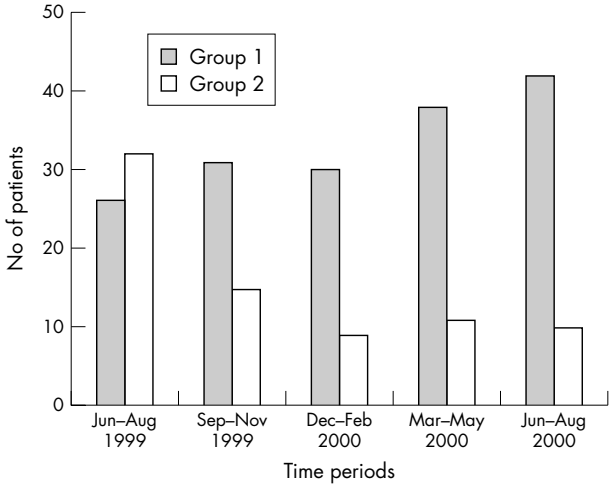

Figure 2 Proportion of patients undergoing total arterial revascularisation over three month periods.

Indication for total arterial revascularisation

A policy of total arterial revascularisation was begun in June 1999 after the publication of the Cleveland Clinic study in May 1999 reporting that two ITA grafts offered significant clinical and survival advantages over one ITA graft in patients undergoing CABG.[8] That report did not address the concept of total arterial revascularisation as it used arterial as well as vein grafts. Our series included patients undergoing urgent surgery (that is, patients with unstable angina requiring surgery on that admission) who constituted over 40% of this surgical population.

Contraindications to total arterial revascularisation

Initially we considered that there were several contraindications to total arterial revascularisation:

- Significantly impaired ventricular function (ejection fraction <30%) because of the likelihood of requiring inotropes (which predispose to arterial graft spasm) and a limited life expectancy.
- Patients on angiotensin converting enzyme (ACE) inhibitors which predispose to a vasoplegic state after cardiopulmonary bypass and may require vasoconstrictors (which predispose to arterial graft spasm).
- Obese insulin dependent diabetics (but not diabetics with a normal body mass index), because of increased risk of sternal problems with bilateral ITA grafts.
- An abnormal Allen test as a contraindication to the use of the radial artery.

Surgical techniques

Preparation of conduits

Patients undergoing total arterial revascularisation had all grafts performed using a combination of the left ITA, right ITA, and radial artery. The ITA conduits were harvested with a skeletonised rather than a pedicled technique to decrease the risk of sternal devascularisation,[18] and latterly the radial artery was also harvested in a skeletonised fashion.[19] The ITA were treated topically with papaverine to prevent spasm and the radial artery irrigated internally and externally with 100 mg phenoxybenzamine in 50 ml of blood as previously described.[20]

Cardiopulmonary bypass

Most operations were performed with cardiopulmonary bypass but in the latter part of the study a few operations were performed as beating heart procedures. Cardiopulmonary bypass was achieved using a pump flow rate of 2.4 l/m^2/min at normothermia with temperature allowed to drift to 34°C. Topical cooling was not used, and the side limb of the cardioplegia cannula was used for venting. A Cobe CML membrane oxygenator (Cobe Cardiovascular Inc, Arvada) and a roller pump producing non-pulsatile flow were used without an arterial line filter. Alpha stat control of acid-base management was used and the mean arterial pressure maintained between 50 and 60 mm Hg with pharmacological manipulation if necessary.

Myocardial protection

All anastomoses were constructed during a single cross clamp period with one litre of St Thomas's cold (4°C) crystalloid cardioplegia administered every 30 minutes as necessary.

Graft distribution

Various distributions of the grafts were used based on the principle of placing both ITA grafts to the left sided coronary vessels. This included the use of left ITA to the left anterior descending coronary artery and right ITA to the obtuse marginal artery via the transverse sinus with the radial artery placed to the posterior descending artery. More recently the left ITA has been placed to the obtuse marginal artery and the right ITA to the left anterior descending coronary artery. The proximal anastomosis ("top ends") of the radial artery were initially performed on the aorta but more recently as composite grafts to the right ITA or left ITA in a "T" or "Y" fashion (see fig 1).

Conventional CABG was performed using the left ITA to the left anterior descending coronary artery and supplemental vein grafts as necessary. Proximal venous anastomoses were placed on the aorta.

Statistical methods

Analysis was performed using SPSS (version 9.0). Normally distributed data are presented as mean and standard deviation and comparisons undertaken with a non-paired *t* test. Categorical data were compared with a χ^2 test. A p value of <0.05 was considered as the conventional level of statistical significance.

RESULTS

Over a period of 17 months from June 1999 until the end of October 2000, of 245 patients undergoing first time CABG by one surgeon (DPT), 165 (67%) underwent total arterial revascularisation (group 1) and 80 (33%) had conventional CABG (group 2). The proportion of patients receiving total arterial

Table 1 Preoperative data

	Total (n=245)	Group 1 (n=165)	Group 2 (n=80)	p Value
Mean (SD) age	62 (10)	60 (10)	66 (9)	<0.001
Female patients (%)	32 (13)	16 (10)	16 (20)	0.04
Mean (SD) body mass index	27 (4)	27 (3)	27 (4)	0.3
Urgent (%)	105 (43)	67 (41)	38 (47)	0.3
Mean (SD) Parsonnet score	7 (6)	5 (5)	11 (7)	<0.001
Ventricular function (%)				
EF >50%	138 (57)	101 (61)	37 (46)	
EF 30%–49%	75 (30)	54 (35)	21 (27)	
EF <30%	32 (13)	10 (6)	22 (27)	<0.05
Smoking (%)	31 (13)	21 (12)	10 (13)	0.9
Diabetes (%)	46 (19)	29 (18)	17 (21)	0.6
Hypertension (%)	129 (53)	79 (48)	50 (62)	0.06
Mean (SD) creatinine (mmol/l)	110 (37)	109 (41)	111 (25)	0.7
Creatinine >150 mmol/l (%)	9 (3.7)	4 (2.4)	5 (6)	0.7

EF, ejection fraction.

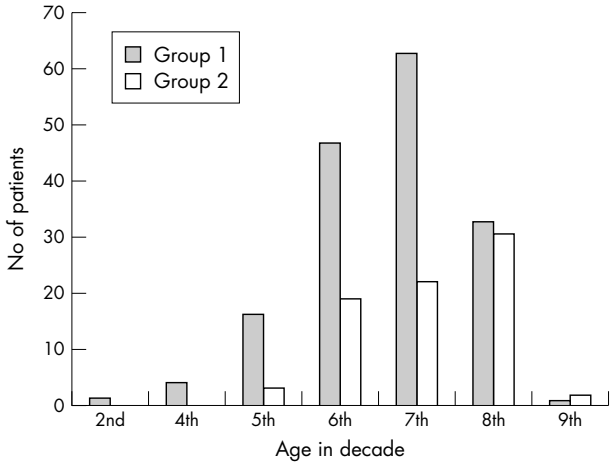

Figure 3 Age of patients in decades in both groups.

revascularisation increased from 44% of patients in the first three month period of the study to 67% in the second three month period and more than 75% of the cases over the three latest three month periods (fig 2). This reflected a combination of growing confidence with the technique and the demonstration that phenoxybenzamine prevented radial artery spasm[20] so that preoperative use of ACE inhibitors was no longer considered a contraindication.

Preoperative data

As shown in table 1 patients in group 2 were older (see fig 3), contained a higher proportion of females, and had a higher Parsonnet score. Poor ventricular function (ejection fraction <30%) was present in 22 (27%) patients in group 2 and 10 (6%) patients in group 1. The proportion of urgent patients (that is, those with unstable angina requiring surgery on that admission) was similar in both groups.

Intraoperative data

Each group received the same number of grafts with group 1 receiving a mean (SD) of 2.8 (0.7) grafts and group 2 having 2.9 (0.7) grafts.

Postoperative data

Mortality

The 30 day mortality was three patients (1.2%) comprising a single patient (0.6%) in group 1 and two patients (2.5%) in group 2 (see table 2).

The group 1 patient who died was a 60 year old male asthmatic who had undergone urgent bilateral ITA grafting for a tight left main stem stenosis without cardiopulmonary bypass. He had been extubated early after surgery but 36 hours later had deteriorating respiratory status. Unsuccessful attempts at reintubation resulted in cardiac arrest from which the patient could not be resuscitated. Postmortem examination showed both grafts to be patent.

Two patients died in group 2. One was an 80 year old woman who suffered an extensive anterior myocardial infarct and continued to have chest pain underwent urgent CABG. She died 24 hours after surgery from low cardiac output despite inotropic support and an intra-aortic balloon pump. Postmortem examination confirmed extensive infarction and that both grafts were patent.

The other patient in group 2 was a 76 year old man who underwent urgent CABG for unstable angina with one ITA and one vein graft. He developed a low cardiac output syndrome, which was unresponsive to all supportive measures and died of multiorgan failure on the fourth postoperative day. Postmortem examination showed no recent infarct and that both grafts were patent.

Reopening for bleeding

Six patients (2.4%), of whom three had undergone urgent CABG, required re-exploration for bleeding (see table 2). The single patient (0.6%) in group 1 was bleeding from a side branch of the radial artery and of five patients (6%) in group 2, four had diffuse "coagulopathic" bleeding without a specific bleeding point.

Sternal dehiscence

Four patients (1.6%), three patients in group 1 (1.8%) and a single patient (1.3%) in group 2, developed sternal dehiscence (see table 2). Three of these patients had undergone urgent CABG for unstable angina. The group 1 patients developing sternal dehiscence were:

- A 56 year old male asthmatic undergoing urgent CABG who required prolonged ventilation for severe respiratory infection and dialysis for temporary renal failure.
- A 52 year old Asian male diabetic who had urgent CABG for postinfarction unstable angina. He also had severe haemoptysis from pulmonary aspergillosis in a healed tuberculous cavity.
- A 68 year old male asthmatic undergoing elective CABG had an inadvertent paramedian sternotomy (and the right ITA was not harvested). He required prolonged ventilation for chest infection, complicated by pulmonary embolism, and required tracheostomy for weaning.

The only group 2 patient with sternal dehiscence was a morbidly obese (body mass index 35) 47 year old diabetic woman who continued to smoke before urgent CABG.

Table 2 Postoperative data

Descriptive	Total (n=245)	Group 1 (n=165)	Group 2 (n=80)	p Value (group 1 v 2)
30 Day mortality (%)	3 (1.2)	1 (0.6)	2 (2.4)	0.2
Reopening (%)	6 (2.4)	1 (0.6)	5 (6)	0.008
Cerebrovascular accident (%)	1 (0.4)	1 (0.6)	0	0.98
Supraventricular tachycardia (%)	34 (14)	26 (16)	8 (10)	0.2
Mean (SD) creatinine (mmol/l)	124 (73)	118 (70)	134 (78)	0.1
Creatinine >150 mmol/l (%)	32 (13)	16 (10)	16 (20)	0.8
Dialysis required (%)	5 (2)	2 (1.2)	3 (3.6)	0.2
Sternal dehiscence (%)	4 (1.6)	3 (1.8)	1 (1.3)	0.8
Median (IQ) length of stay (days)	5 (4–7)	5 (4–6)	5 (5–7)	0.06

IQ, interquartile range.

Stroke

One patient (0.6%) developed stroke in group 1. It occurred in a 71 year old obese hypertensive patient who had inadvertent carotid artery puncture during central venous line insertion. A 69 year old arteriopathic man with asymptomatic bilateral internal carotid artery stenosis of >90% had paraplegia after intra-aortic balloon insertion.

Renal failure

Nine patients had impaired renal function (plasma creatinine >150 mmol/l) preoperatively and 32 postoperatively (see table 2). Of five patients (two in group 1 (1.2%) and three in group 2 (3.8%)) who required postoperative haemofiltration three had preoperative renal impairment.

Postoperative stay

The median length of stay was five days in both groups (see table 2), but the interquartile range was shorter in group 1 patients just failing to reach statistical significance (p= 0.06).

DISCUSSION

The aim of this study was to assess the feasibility of total arterial revascularisation as a primary strategy for CABG in a typical UK surgical practice and not to compare total arterial revascularisation and conventional CABG. Specifically we report our results to address persistent concerns that such a strategy might increase perioperative mortality and morbidity. To the best of our knowledge no similar strategy or study has been reported from the UK.

The most obvious weaknesses of our study are the lack of angiographic and long term clinical follow up. Although neither was the primary aim of this study, inferences about both can be drawn from the literature. It is increasingly clear that the long term patencies of ITA anastomoses to all coronary vessels, rather than simply the left anterior descending coronary artery, are superior to those achievable with vein grafts.[15 16] Calafiore and colleagues reported that >95% of ITA grafts to all left sided coronary vessels were patent 18 months after CABG.[15] More importantly, Dion and colleagues reported that 96% of ITA anastomoses to all coronary vessels were patent seven years after CABG in 161 patients who consented to repeat angiography.[16] The best available evidence suggests that radial arteries also have superior patency to vein grafts five years after CABG,[21 22] but it is unknown whether they will achieve the outstanding patency rates of ITA grafts.

Even in the absence of randomised trials of arterial revascularisation versus conventional CABG, there is evidence of clinical and survival benefit with bilateral ITA grafting. In May 1999 the Cleveland clinic group reported that bilateral ITA grafts improved 10–15 year survival and markedly reduced the need for reoperation.[8] These benefits were also present in patients of advanced age, and in those with diabetes or significantly impaired ventricular function.[8] In contrast, Sergeant and colleagues reported no survival benefit of bilateral ITA grafting.[23] One possible explanation for this, however, is that of their database of 9600 patients only around 100 with bilateral ITA grafts have been followed up to 10 years and in their early experience the second ITA graft was frequently used to the anatomically less important diagonal coronary artery.[23] In a recent meta-analysis of almost 16 000 patients matched for age, gender, left ventricular function, and diabetes we reported that the bilateral ITA group had significantly better survival (hazard ratio for death=0.81, 95% confidence interval 0.70 to 0.94).[17]

The most important finding in our study is that total arterial revascularisation can be performed in most patients undergoing CABG in a typical UK population with an acceptably low mortality and morbidity. While these were not our highest risk patients, they were not a specially selected low risk group. Their mean age was 60 years but 21% were over 70 years (and one was over 80 years), 40% were urgent patients, and approximately one fifth had diabetes.

It is also apparent that with increasing surgical experience the proportion of patients who are suitable candidates for total arterial revascularisation increases. In our own practice this rapidly increased from 44% in the earlier part of the study to over three quarters of patients in the latter periods (and is currently over 90%). This was also a consequence of laboratory based evidence that phenoxybenzamine effectively abolishes radial artery spasm.[20] This is a particularly relevant consideration as radial arteries are more prone to spasm than other conduits including the ITA and particularly in the presence of α-adrenergic mediated constriction.[24] The appeal of phenoxybenzamine lies in the fact that it can be applied as a topical solution to the radial artery (avoiding systemic side effects of hypotension), binds irreversibly to α-receptors and does not damage endothelial function.[20] This significantly increased our scope of use of the radial artery to those patients on preoperative ACE inhibitors (who frequently require vasoconstrictors in the postoperative period) and those patients who might require modest doses of inotropes after surgery. Indeed, our only persisting contraindication to the use of arterial grafts is in patients with severely impaired left ventricular function who have a more limited life expectancy and who are likely to need an intra-aortic balloon and/or significant inotropic support after surgery.

The incidence of sternal dehiscence, the most feared complication of the use of both ITA, was similar in both groups. We would emphasise that harvesting ITA conduits in a skeletonised rather than pedicled fashion significantly reduces the risk of sternal devascularisation by preserving ITA collaterals to the chest wall.[18 25] Although it occurred in three (1.8%) of our group 1 patients, only two had bilateral ITA grafts (the third patient had a single ITA and sequential radial artery because a paramedian sternotomy had inadvertently been performed). In the two patients who developed sternal dehiscence both had significant pre-existing respiratory problems: one asthmatic required prolonged ventilation for

respiratory infection and the other, an insulin dependent diabetic of 40 years standing, had pulmonary aspergillosis in an old tuberculous cavity.

We do not consider that diabetes is a contraindication to the use of skeletonised ITA grafts unless the patient is also obese. Approximately one fifth of our patients were diabetic and recent evidence from the BARI trial suggests that such patients have most to gain from the use of bilateral ITA grafts.[26]

It is also noticeable that only a single patient in group 1 required re-exploration for bleeding in comparison to five patients in group 2, although over 40% of patients in both groups underwent urgent surgery. The most likely explanation for this discrepancy is that group 1 patients routinely received aprotonin, as we have previously demonstrated that there is an increased tendency to blood loss in these patients.[27] In a previous study, the mean (SD) blood loss in patients receiving bilateral ITA was 1324 (362) ml compared with 945 (330) ml in patients receiving a single ITA ($p<0.001$).[27] However, we acknowledge that chest closure was routinely undertaken by the consultant in group 1 patients (because of the perceived increase in risk of sternal dehiscence) whereas it was frequently performed by trainee surgeons in patients receiving the conventional operation.

Another surgical consideration is the increased length of operating time required to perform total arterial revascularisation. In the authors' hands this increases total surgical operating time from around one hour and 55 minutes in group 2 patients to around two hours and 40 minutes in group 1 patients. The increase in operative time is necessary for harvesting the grafts and not cardiopulmonary bypass times, which are 69 (12) minutes for group 1 patients and 65 (20) minutes for group 2 patients.[27]

In contrast to earlier reports[28 29] we demonstrated, using sensitive biochemical markers of myocardial damage such as troponin-T that the use of both ITA grafts does not predispose to myocardial injury.[30] Indeed, the risk of perioperative myocardial injury might be reduced with total arterial revascularisation because of a decreased likelihood of early vein graft failure.

A further concern with bilateral ITA grafting is an increased risk of pleuropulmonary morbidity.[31 32] While bilateral ITA grafting does impair chest wall mechanics it does not exacerbate functional respiratory exchange. Indeed we reported that bilateral ITA grafting does not increase the respiratory impairment as judged by serial blood gases after cardiac surgery.[33]

Total arterial revascularisation offers further advantages over conventional CABG. The use of in situ or composite bilateral ITA grafts (with an additional radial artery) eliminates the need to perform "top ends" on the aorta. It is manipulation of the aorta by cannulation, or with a cross clamp or side biting clamp, which is a major cause of stroke after CABG. Furthermore total arterial revascularisation is particularly suitable for patients without adequate saphenous vein, and eliminates the frequently underestimated morbidity associated with harvesting vein from the legs. Finally, total arterial revascularisation is compatible with, and may indeed facilitate, the rapidly increasing techniques of CABG without cardiopulmonary bypass (off-pump or OPCAB).[34]

CONCLUSION

Total arterial revascularisation is a feasible primary strategy in most patients presenting for first time CABG and can be performed with low mortality and morbidity.

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I am pleased to inform authors and reviewers of *Postgraduate Medical Journal's* new online submission and review system. *Bench>Press* is a fully integrated electronic system which uses the internet to allow rapid and efficient submission of manuscripts, and the entire peer review process to be conducted online.

Authors can submit their manuscript in any standard word processing software. Graphic formats acceptable are: .jpeg, .tiff, .gif, and .eps. Text and graphic files are automatically converted to PDF for ease of distribution and reviewing purposes. Authors are asked to approve their submission before it formally enters the reviewing process.

To access the system click on "SUBMITTING YOUR MANUSCRIPT" on the *PMJ* homepage: http://www.postgradmedj.com/ or you can access *Bench>Press* directly at http://submit-pmj.bmjjournals.com/.

We are very excited with this new development and we would encourage authors and reviewers to use the online system where possible. It really is simple to use and should be a big improvement on the current peer review process. Full instructions can be found on *Bench>Press* and *PMJ online*. Please contact Natalie Davies, Project Manager, ndavies@bmjgroup.com for further information.

Pre-register with the system

We would be grateful if all *PMJ* authors and reviewers pre-registered with the system. This will give you the opportunity to update your contact and expertise data, allowing us to provide you with a more efficient service.

Instructions for registering

1. Enter http://submit-pmj.bmjjournals.com.
2. Click on "Create a new account" in the upper left hand side of the *Bench>Press* homepage.
3. Enter your email address in the space provided.
4. Choose a password for yourself and enter it in the spaces provided.
5. Complete the question of your choice to be used in the event you cannot remember your password at a later time *(this will be needed if you forget your password)*.
6. Click on the "Complete step 1" button at the bottom of the screen.
7. Check the email account you registered under. An email will be sent to you with a verification number and URL.
8. Once you receive the email, copy the verification number and click on the URL hyperlink. Enter the verification number in the relevant field. Click on "Verify me". This is for security reasons and to check that your account is not being used fraudulently.
9 . Enter/amend your contact information, and update your expertise data.