

# High Thoracic Epidural Analgesia Reduces the Risk of Long-Term Depression in Patients Undergoing Coronary Artery Bypass Surgery

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**Background:** High thoracic epidural analgesia (HTEA) has been shown to reduce psychological morbidity in the early period following coronary artery bypass graft surgery (CABG). Our aim was to identify whether the effect persists in the longer term.

**Materials and Methods:** Patients from a previous randomised study of HTEA for CABG were followed up 6 months to 3 years following surgery. The cardiac depression scale (CDS) was used to identify severity of depression.

**Results:** Sixty-one of the original 78 patients were able to participate in the study. Eight point three percent of patients had CDS scores >100, consistent with severe depression (1 epidural patient, 4 control patients,  $P=0.353$ ). After adjustment for time of follow-up, the CDS scores in patients who received HTEA were significantly lower ( $66\pm 3.5$ ) than patients who received intravenous morphine analgesia ( $79\pm 3.5$ )  $P<0.05$

**Conclusion:** The use of HTEA results in a lower risk of depression 6 months or more following CABG. (Ann Thorac Cardiovasc Surg 2007; 13: 32–5)

**Key words:** high thoracic epidural analgesia, coronary artery bypass surgery, depression

## Introduction

Pain following coronary artery bypass graft surgery (CABG), is reported as moderate to severe in two thirds of patients, especially with respiratory effort.<sup>1)</sup> Royse et al.<sup>2)</sup> conducted a randomised trial of high thoracic epidural analgesia (HTEA) versus patient controlled analgesia using morphine in patients undergoing CABG. They reported significantly lower pain scores both at rest and with coughing. The use of HTEA greatly reducing pain in the

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majority of patients. There was a significantly lower incidence of depression and symptoms of post-traumatic stress disorder at follow-up 6 weeks following surgery. The concept that pain following surgery can affect the development of postoperative psychological morbidity is a poorly investigated area of cardiac surgery, but could account in part for the high incidence of neuropsychological disorder that occurs following CABG.<sup>3)</sup>

Our aim was to identify whether differences in depression related to the use of HTEA persisted in the longer term.

## Materials and Methods

Institutional ethics committee approval was obtained to extend a study that assessed the effects of analgesia technique on short-term postoperative psychological recovery from CABG. Written informed patient consent was obtained. The original investigation was conducted on 80 CABG patients who were randomised to receive HTEA

or a patient controlled intravenous morphine analgesia (control) for 3 days following surgery.<sup>2)</sup>

In the current study, patients were followed-up between 6 months to 3 years after CABG surgery in order to assess long-term psychosocial outcomes, using a questionnaire containing psychometric measures. Patients were given the option of being mailed the questionnaire and completing it on their own, or being visited by the researcher and assisted in completing the questionnaire. The researcher visited 39% patients to assist in the completion of the questionnaire.

### Depression measure

Depression was the primary psychosocial endpoint assessed. The cardiac depression scale (CDS) was included in the questionnaire to provide a sensitive measure of depression that is specific for cardiac populations.<sup>4)</sup> The CDS consists of 26 items that measure 7 factors: sleep, anhedonia, uncertainty, mood, cognition, hopelessness and inactivity. There are 7 positively worded items and 19 negatively worded items, which were presented in a mixed order and were assessed on a 7-point Likert scale (1 = strongly disagree, 7 = strongly agree). Higher scores indicate worse function. The CDS has been found to have high reliability and validity in a population of cardiac outpatients with a range of diagnoses, and a score greater than 100 is consistent with severe depression.<sup>4)</sup> In the original study, the Minnesota Multiphasic Personality Inventory (MMPI) 2 was used to assess depression and posttraumatic stress disorder using subscales.

### Statistical methods

Descriptive information are summarised as group mean  $\pm$  standard error (SE). One-way analysis of covariance (ANCOVA) was used to analyse the effect of analgesia on depression scores, whilst controlling for time of follow-up. Time of follow-up was measured as the number of months after CABG surgery. Statistical significance was attained if the 2-sided  $P=0.009$ . Data was analysed using SPSS V13.0 (SPSS Inc., Chicago, IL).

### Results

Attempts were made to contact 78 patients who participated in the original randomised controlled trial. Eight patients were unable to be contacted via phone or mail, 5 patients declined participation, 2 patients were seriously ill, 1 patient could not participate due to limited English and 1 patient had died (following hospital discharge,

from small bowel infarction). There were no demographic differences between groups in the original study, and all cases were CABG. In the early postoperative course, there were no strokes or deep space infections.

Sixty-one patients participated in the current follow-up study. Data from 1 patient were excluded because of cognitive impairment. There were 49 males (mean age =  $64.6 \pm 1.3$  years) and 11 females ( $70.3 \pm 2.9$  years). The range of follow-up was 6.6–36 months (mean = 22.72, standard deviation (SD) = 9.24 months).

Severe depression at postoperative follow-up (CDS > 100) was reported in only 8.3% of all patients (1 epidural group, 4 control group,  $P=0.353$ ). After adjustment for time of follow-up, the CDS scores in patients who received HTEA were significantly lower ( $66 \pm 3.5$ ) than patients who received intravenous morphine analgesia ( $79 \pm 3.5$ ),  $P < 0.05$ .

### Comment

This study shows that the incidence of long-term severe depression is relatively low in patients undergoing CABG. Differences in depression score severity, however, are present 6 months or longer following CABG, and are reduced in patients who received HTEA. This finding suggests that pain is a traumatic experience that results in psychological morbidity extending well beyond hospital discharge.

The use of HTEA provides excellent analgesia to the majority of patients, whereas there is much greater variation in the quality of analgesia using conventional opioid based techniques.<sup>2)</sup> Previous studies investigating HTEA for cardiac surgery have demonstrated improvement in pain, but have focused on identifying differences in morbidity or complications such as lung function,<sup>5,6)</sup> arrhythmia,<sup>6)</sup> stress response,<sup>7)</sup> or myocardial damage.<sup>7-9)</sup> This is the first report to identify that use of HTEA for CABG is associated with a reduced risk of depression in the medium to longer time frame.

HTEA use in cardiac surgery has been controversial because of a theoretical increased risk of epidural haematoma<sup>10)</sup> associated with systemic anticoagulation.<sup>11)</sup> There is now worldwide experience with HTEA with over 8,000 cases reported<sup>11,12)</sup> and many other institutions who have not reported series,<sup>13)</sup> without an increased incidence of epidural haematoma. There has been 1 case reported in the paediatric population, where an epidural haematoma occurred following use of antithrombotic and anticoagulant therapy in association with catheter manipulation,

which was successfully treated without permanent neurological sequelae.<sup>14)</sup> This data indicates that the risk of epidural haematoma in cardiac surgery is unlikely to be any different from epidural use in other forms of surgery including use in labour. It is important to consider morbidity of alternative analgesic techniques. Whilst opioid therapies are considered safe, they are not without risk or complication. Acute pain service audit data, suggests that the incidence of potentially life-threatening complications using PCA opioid therapy is approximately 1:300 cases.<sup>15)</sup> Non-steroidal anti-inflammatory drugs (especially, cyclooxygenase (COX) 2 inhibitors), though excellent analgesics, have recently been shown to worsen cardiovascular risk, leading to withdrawal of medications such as rofecoxib, and indications removed for cardiac surgery for parecoxib. The risk of analgesia related complications is low in comparison to the overall risk of cardiac surgery, and arguably, there is little difference in risk for serious complications between HTEA and other analgesic therapies.

There are several limitations to this study. First, we were unable to follow up the entire cohort from the original study. It is possible that some of the patients who refused participate may have been more severely depressed, and therefore biasing the study towards patients with better psychological health. We also used a different psychological rating tool in our follow-up study. In the original study we found the MMPI 2 to be a very cumbersome psychological tool with considerable reluctance from patients to participate in it during follow-up. The CDS is a much simpler and faster test to complete, and importantly, it has been validated in the same patient population as this study (Melbourne, Australia). The CDS was designed to investigate “adjustment disorder with depressed mood” rather than depression in a psychiatric population, which is important when considering different patient populations (acute medical rather than psychiatric). The CDS has also been shown to have excellent responsiveness to change and test — retest reliability. It has a normal distribution of scores compared with a markedly skewed distribution seen with psychiatric based tests (such as the Beck Depression Inventory).<sup>4)</sup> For these reasons we chose the CDS over Beck depression inventory or MMPI 2 as our follow-up measurement, although a disadvantage of using different rating tools was that pre-operative CDS scores could not be accounted for in this study. However, we believe that the CDS is a better validated tool in cardiac surgery patients. Although the value of 100 is indicative of severe depression, there are no cut

off scores for mild or moderate depression. The normal distribution of scores, however, makes it likely that a higher value will indicate a greater degree of depression.

## Conclusion

The use of HTEA results in a lower risk of depression 6 months or more following CABG.

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