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[Intervention Review]

Anaesthetic techniques for risk of malignant tumour recurrence

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ABSTRACT

Background

Surgery remains a mainstay of treatment for malignant tumours; however, surgical manipulation leads to a significant systemic release of tumour cells. Whether these cells lead to metastases is largely dependent on the balance between aggressiveness of the tumour cells and resilience of the body. Surgical stress per se, anaesthetic agents and administration of opioid analgesics perioperatively can compromise immune function and might shift the balance towards progression of minimal residual disease. Regional anaesthesia techniques provide perioperative pain relief; they therefore reduce the quantity of systemic opioids and of anaesthetic agents used. Additionally, regional anaesthesia techniques are known to prevent or attenuate the surgical stress response. In recent years, the potential benefit of regional anaesthesia techniques for tumour recurrence has received major attention and has been discussed many times in the literature. In preparing this review, we aimed to summarize the current evidence systematically and comprehensively.

Objectives

To establish whether anaesthetic technique (general anaesthesia versus regional anaesthesia or a combination of the two techniques) influences the long-term prognosis for individuals with malignant tumours.

Search methods

We searched *The Cochrane Library* (2013, Issue 12), PubMed (1950 to 15 December 2013), EMBASE (1974 to 15 December 2013), BIOSIS (1926 to 15 December 2013) and Web of Science (1965 to 15 December 2013). We handsearched relevant websites and conference proceedings and reference lists of cited articles. We applied no language restrictions.

Selection criteria

We included all randomized controlled trials or controlled clinical trials that investigated the effects of general versus regional anaesthesia on the risk of malignant tumour recurrence in patients undergoing resection of primary malignant tumours. Comparisons of interventions consisted of (1) general anaesthesia alone versus general anaesthesia combined with one or more regional anaesthetic techniques; (2) general anaesthesia combined with one or more regional anaesthetic techniques; and (3) general anaesthesia alone versus one or more regional anaesthetic techniques. Primary outcomes included (1) overall survival, (2) progression-free survival and (3) time to tumour progression.

Data collection and analysis

Two review authors independently scanned the titles and abstracts of identified reports and extracted study data.

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All primary outcome variables are time-to-event data. If the individual trial report provided summary statistics with odds ratios, relative risks or Kaplan-Meier curves, extracted data enabled us to calculate the hazard ratio using the hazard ratio calculating spreadsheet. To assess risk of bias, we used the standard methodological procedures expected by The Cochrane Collaboration.

Main results

We included four studies with a total of 746 participants. All studies included adult patients undergoing surgery for primary tumour resection. Two studies enrolled male and female participants undergoing major abdominal surgery for cancer. One study enrolled male participants undergoing surgery for prostate cancer, and one study male participants undergoing surgery for colon cancer. Follow-up time ranged from nine to 17 years. All four studies compared general anaesthesia alone versus general anaesthesia combined with epidural anaesthesia and analgesia. All four studies are secondary data analyses of previously conducted prospective randomized controlled trials.

Of the four included studies, only three contributed to the outcome of overall survival, and two each to the outcomes of progression-free survival and time to tumour progression. In our meta-analysis, we could not find an advantage for either study group for the outcomes of overall survival (hazard ratio (HR) 1.03, 95% confidence interval (CI) 0.86 to 1.24) and progression-free survival (HR 0.88, 95% CI 0.56 to 1.38). For progression-free survival, the level of inconsistency was high. Pooled data for time to tumour progression showed a slightly favourable outcome for the control group (general anaesthesia alone) compared with the intervention group (epidural and general anaesthesia) (HR 1.50, 95% CI 1.00 to 2.25).

Quality of evidence was graded low for overall survival and very low for progression-free survival and time to tumour progression. The outcome of overall survival was downgraded for serious imprecision and serious indirectness. The outcomes of progression-free survival and time to tumour progression were also downgraded for serious inconsistency and serious risk of bias, respectively.

Reporting of adverse events was sparse, and data could not be analysed.

Authors' conclusions

Currently, evidence for the benefit of regional anaesthesia techniques on tumour recurrence is inadequate. An encouraging number of prospective randomized controlled trials are ongoing, and it is hoped that their results, when reported, will add evidence for this topic in the near future.

PLAIN LANGUAGE SUMMARY

Anaesthetic techniques for risk of malignant tumour recurrence

Background

Surgery remains a mainstay of treatment for patients with many types of cancer. However, surgical stress and certain anaesthesia and pain medications commonly given during anaesthesia for cancer surgery are known to suppress body defences. Therefore, surgery and anaesthesia might contribute to long-term cancer recurrence. Different types of anaesthesia are available. General anaesthesia indicates that the patient goes to sleep for his or her surgery, regional anaesthesia means that the part of the body that is operated on is numbed by a numbing medication (local anaesthetic), or a combination of the two techniques can be used. Regional anaesthesia has the potential to reduce the use of certain anaesthesia and pain medications that are injected into the vein or inhaled into the lung, as well as to attenuate surgical stress. Therefore, previous research has suggested that regional anaesthesia might reduce the risk of long-term cancer recurrence.

Research question

We aimed to discover whether different types of anaesthesia used during cancer surgery could influence long-term survival or the rate of tumour recurrence in patients undergoing cancer surgery.

Search date

Evidence is current to December 2013.

Study characteristics

We found four studies with a total of 746 adult men and women undergoing abdominal surgery for removal of cancer. All studies were reanalyses of previously conducted trials, which means that none of the included studies was actually designed to investigate tumour recurrence. All patients underwent primary cancer surgery, which means that surgery on cancer metastases was not included. A total of 354 participants received general anaesthesia and 392 participants received a general anaesthesia along with an epidural anaesthesia. Epidural anaesthesia is a certain type of regional anaesthesia by which a numbing medication is injected continuously via a catheter into the epidural space. The epidural space serves as the outermost surrounding of the spinal cord. Numbing medication injected into the epidural space causes certain parts of the belly area to go numb and be insensitive to pain. Study participants were followed for at least 7.8 years after they had undergone cancer surgery.

Key results

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We did not find a benefit for either study group on cancer recurrence or survival. Because of incomplete reporting and the low number of reported adverse events, we cannot estimate possible differences in adverse effects between the different anaesthesia techniques used.

Quality of the evidence

The quality of the evidence for outcomes was graded low for overall survival and very low for progression-free survival and time to tumour progression. The main limitations of the evidence we identified were that the results could have been influenced by the background treatments given to people who participated in the trials.