

Peer Review File

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REVIEWER 1

Comments to the authors:

A very good review of the current evidence into propofol-TIVA versus inhalational anesthesia for cancer surgery. Please consider:

- **Comment 1.** Commenting on the systematic review

Soltanizadeh S et al, Outcomes of cancer surgery after inhalation and intravenous anaesthesia: a systematic review. Journal of clinical Anesthesia 2017; 42:19-25

- **Reply 1:** Added in sentence and reference referring to this systematic review under ‘Clinical Studies’ heading when discussing meta-analyses/systematic reviews – paragraph starting line 282 in pdf.

- **Comment 2.** Altering line 198- adding the word ‘are’?

- **Reply 2:** As per line 198 in the PDF document, I have added the words ‘that are’ so the sentence reads correctly. It now reads as “Many utilized anesthetic agents THAT ARE no longer used clinically and *in vitro* conditions remove the cellular environment a cancer cell inhabits and eliminate the host’s immune system response.”

REVIEWER 2

Comments to the authors:

The paragraphs on ‘Anaesthesia and cancer cell biology’ and ‘Clinical evidence’ list a lot of studies rather than relating them specifically to how we can modify our anaesthetics - the summary paragraphs at the end is useful but maybe all the studies aren’t needed to be listed or could be presenting more clearly in an ‘evidence against use of inhalationals’ or ‘evidence for TIVA’ to make it a bit clearer as you read through it.

Reply: We have added an introduction sentence to the paragraphs in the ‘Anesthesia and cancer cell biology’ section to make it clearer that we are discussing the evidence against the use of inhalational anesthesia followed by the evidence for propofol-TIVA. The overall point we have tried to make in the paper is that though there are multiple low powered studies suggesting a benefit in cancer outcomes with propofol-TIVA, at

present there is not strong robust clinical evidence in prospective randomized controlled trials to support either technique and we need to await results from ongoing research trials (specified in table 1). Hence, we feel it would be unreasonable to advise how to modify the anaesthetic technique as per the reviewer's comment.

REVIEWER 3

Comments to the authors:

A great summary of a complex topic with lots of conflicting evidence, with a good, pragmatic conclusion.

Specific points:

- **Comment 1:** Does the assertion that obesity is an independent risk factor for the development of cancer, on line 58, need a reference?
- **Reply 1:** Reference (5) added
- **Comment 2:** Is it possible to build a stronger narrative into the paragraph describing animal/cell line studies and volatile anaesthesia (Line 141 onwards), as although important, begins to read like a list of studies, and loses its impact.
- **Reply 2:** We hope by adding in an introduction sentence to the paragraphs discussing animal/cell line studies it makes it clearer that we are discussing the evidence against the use of inhalational anesthesia followed by the evidence for propofol-TIVA and helps build the narrative.
- **Comment 3:** VEGF is introduced at an early stage, yet line 260 onwards begins referring to VEGF-C without any explanation of VEGF-C vs. VEGF.
- **Reply 3:** I have changed line 88 in pdf (or line 113 in word document) to a plural so now reads vascular endothelial growth factors. I have added a brief description when referring to VEGF-C at line 260 in pdf (line 285 in word document) to explain what VEGF-C is.

REVIEWER 4

Comments to the authors:

Well written article. Considers cell biology + animal model evidence