

IMPACT OF ANESTHETIC TECHNIQUE ON OVERALL SURVIVAL AND RECURRENCE FREE SURVIVAL IN CUTANEOUS MELANOMA PATIENTS SUBMITTED TO SENTINEL LYMPH NODE BIOPSY: A RETROSPECTIVE COHORT STUDY PROTOCOL

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INTRODUCTION

Surgery is still the main treatment of many solid tumors. In the last decades, has been a point of debate how perioperative stress response and therapeutic modalities employed interact with tumor evolution after surgery. Specifically, in case of melanoma use of general anesthesia has been implied in a worse overall survival in some previous studies, but results are conflicting. We have designed a protocol to help to solve this issue.

METHODS

A retrospective cohort study was conducted evaluating cutaneous melanoma patients submitted to sentinel lymph node biopsy between May 2000 and April 2010 in National Cancer Institute of Brazil (INCA). Follow up period is 5 years. The objective of the study is to evaluate if there is a relationship between overall and recurrence free survival and anesthetic technique used during sentinel lymph node biopsy procedure. We will analyze the overall and recurrence free survival and aspects of intraoperative care including demographic data, baseline clinical characteristics, staging, type of anesthetic technique, use and type of regional anesthesia, use of inhalation anesthetics, length of surgical procedure, use and dose of dexamethasone, opioid agent used and the dose in morphine oral equivalents, use of NSAIDs and metamizole. We will use for discrete variables proportions and for continuous position and variation measures. For survival analysis, Kaplan Meyer method and logrank to obtain p values. Associations between measures will be evaluated using Pearson Chi-square. Associations with a p value of less than 0,05 will be considered statistically significant.

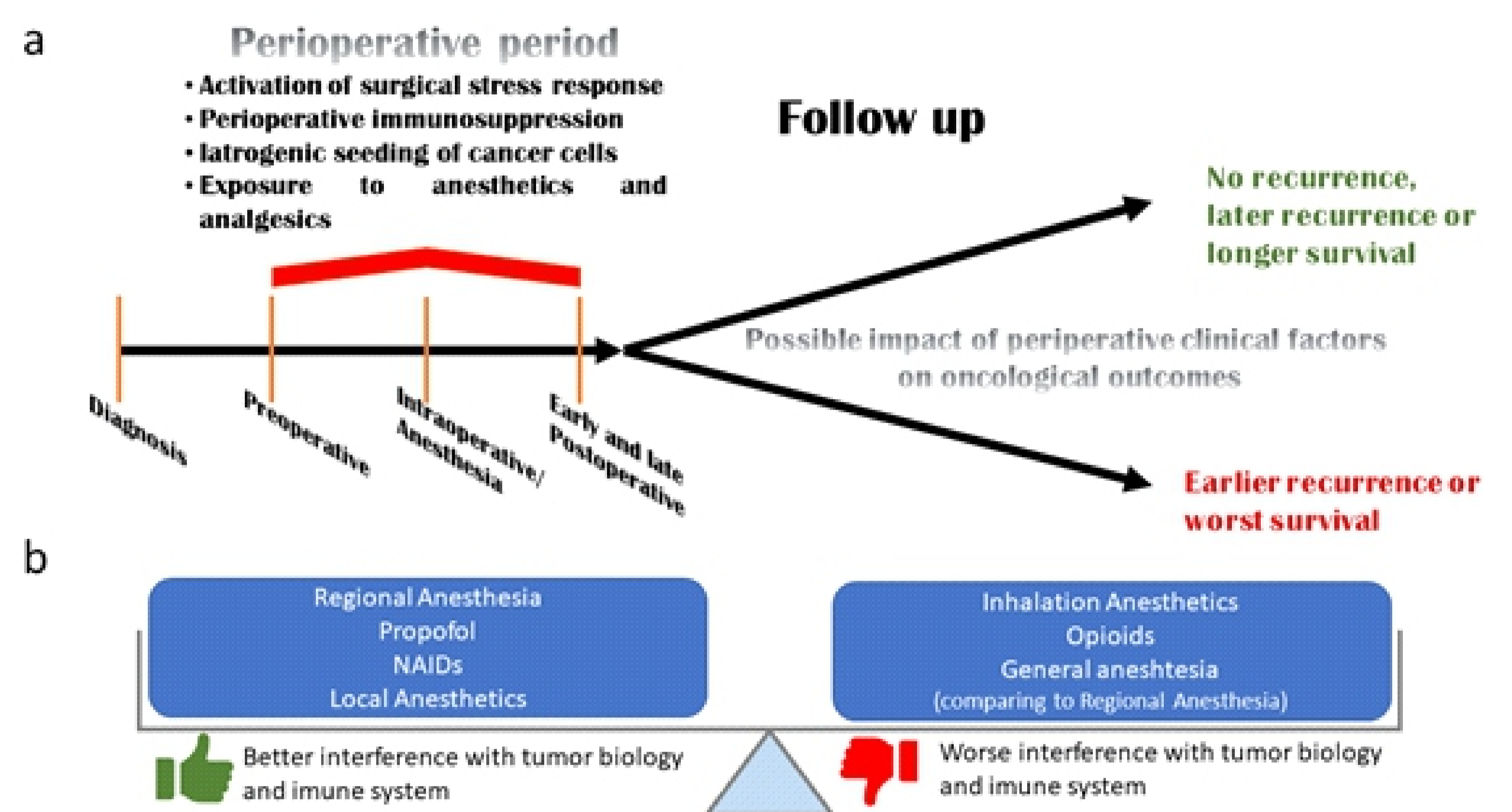


Figure 1 – Perioperative period and oncological outcomes. **a** Time line with diverging outcomes on many possible factors in perioperative period. **b** Balance between some anesthetic agents or techniques associated with a better or worse oncological profit according to previous experimental and clinical data.

DISCUSSION

Previous studies aggregated general anesthesia as a single group, but we believe it lacks a background. Animal studies data support inhalation anesthesia as a pro-metastatic agent in perioperative melanoma setting, but propofol not. Use of local anesthetics in local and regional anesthesia have demonstrated direct cytotoxic activity against cutaneous melanoma cells in vitro. Differently from previous studies in this setting, we will test if there is a dose response relationship between inhalation anesthetics, opioids and dexamethasone intraoperative exposure and outcomes. Thereby, our cohort differs from previous published studies because it was designed specifically to test the relationship between perioperative anesthetic agent exposure and survival endpoints. We tried to minimize such risk of bias during study design.

REFERENCES

1. Kim R. Effects of surgery and anesthetic choice on immunosuppression and cancer recurrence. *J Transl Med.* 2018; 16:8.
2. Kofler L, Breuninger H, Häfner HM et al. Lymph node dissection for melanoma using tumescence local anaesthesia: an observational study. *Eur J Dermatol.* 2018; 28:177-185.
3. Melchi CF, Mele A, Baliva G, Sciò M, Fucci M, Pasquini P, Corona R. Prognostic value of anesthesia type for patients treated for cutaneous melanoma. *Dermatol Surg* 1995;21(9):786-8.
4. Schlagenhauff B, Ellwanger U, Breuninger H, Stroebel W, Rassner G, Garbe C. Prognostic impact of the type of anaesthesia used during the excision of primary cutaneous melanoma. *Melanoma Res* 2000;10(2):165-9.
5. Gottschalk A, Brodner G, Van Aken HK, Ellger B, Althaus S, Schulze HJ. Can regional anaesthesia for lymph-node dissection improve the prognosis in malignant melanoma? *Br J Anaesth* 2012;109(2):253-9.
6. Moudgil GC, Singal DP. Halothane and isoflurane enhance melanoma tumour metastasis in mice. *Can J Anaesth.* 1997; 44:90-4.
7. Shang Z, Feng H, Cui L, Wang W, Fu H. Propofol promotes apoptosis and suppresses the HOTAIR-mediated mTOR/p70S6K signaling pathway in melanoma cells. *Oncol Lett.* 2018; 15:630-634.
8. Kang DK, Zhao LY, Wang HL. Cytotoxic effects of local anesthesia through lidocaine/ropivacaine on human melanoma cell lines. *Braz J Anesthesiol.* 2016; 66:594-602.