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Reply

# Reply letter to: Liposomal bupivacaine reduces narcotic use and time to flatus in a retrospective cohort of patients who underwent laparotomy☆

*Dear Editor,*

Thank you for the interesting comments on our recent article regarding the use of liposomal bupivacaine in laparotomy patients. It is well known that retrospective non-blinded studies have certain limitations, which are acknowledged in our manuscript. In most cases a reasonable attempt was made to mitigate the confounding sources of error due to bias or patient selection. Nevertheless, it is a fair criticism that a significant difference in intra-operative analgesic use may affect post-operative pain control, particularly in the hours immediately post op. However, in most studies this requires different analgesic agents entirely to elicit a small effect between groups [1–3], but despite this fact, in many cases no differences are seen [4,5]. In our study, intra-op anesthesia was at the discretion of the anesthesia team. The same group of anesthesiologists were used to perform the same standard induction (usually with Propofol), maintenance with inhaled anesthetics, and pain control intra-operatively with fentanyl. No differences in practice patterns were introduced by the anesthesia team with the second cohort, no intra-op ketamine or steroids were used. Therefore, while we did not document the intra-op analgesic agents used in this study, we feel that we have mitigated this variable as much as possible by having maintained the same anesthesia practice patterns throughout.

Regarding nurse evaluation of patient pain. Given the fact that pain is subjective, it is not surprising that nurses, anesthesiologists, and patients will have a different evaluation of a given patient's pain scores. However, in our institution and in our study, the nurse elicits the patient's own perception of their pain score using a standardized questionnaire, and the nurse records this numerical value in the medical record. Therefore, this is really a standardized patient-derived evaluation of their pain score. As a result, patient pain scores are actually a secondary question in the study since all patients have control of their PCA narcotics and would be expected to medicate their pain to a satisfactory level. Therefore, the primary endpoint, and most objective measure is how much narcotics the patient needed to reach this satisfactory pain level.

In this study, not all of the endpoints were of equal clinical significance/relevance as the total amount of morphine delivered should be considered the primary endpoint and time to flatus, length of stay and complications as secondary. The section in our methods that suggests we have 4 primary endpoints is unfortunately misleading. Treating all 4 variables as co-primary endpoints would certainly require adjustment for multiple testing. It should be noted, however, that any adjustment in the p-value made to reduce the chance of a type I error will increase the chance of a type II error [6–9]. If we were to do this, it would require a larger sample size to detect a significant effect. Nevertheless, we felt this retrospective study could inform future higher-powered studies seeking to demonstrate clinical efficacy of LB as the primary endpoint.

We appreciate the opportunity to respond to these comments.

Provenance and peer review.

Not Commissioned, internally reviewed.

## Ethical approval

Study was approved by the Institutional Review Board of the Hackensack University Hospital.

## Conflicts of interest

No relevant conflicts of interest are noted for authors Atuhani Burnett, Themba Nyirenda, and Zubin Bamboat. Disclosures for Brian Faley include an education grant from Pacira Pharmaceuticals for pharmacy residency beginning in 2014, employment with Pacira beginning in 2/16/2016, and payment by Pacira for consultation and lectures.

## Funding

None.

## Author contribution

All authors contributed to study design, data collection, analysis, and writing.

## Research registration number (UIN)

No experimental drugs were used. All therapies were FDA approved at the time. Retrospective in design. Study was registered at researchregistry.com, researchregistry4297.

## Guarantor

Zubin Bamboat (senior author), Atuhani Burnett (first author).

## Data statement

- No data contained in this communication.
- Data from the original article available upon request.

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