

## IPTH cost-effectiveness in thyroid surgery

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It is a great privilege and opportunity to respond to Dr. Anand Kumar Mishra.

Concerns raised by the Author are extremely important. We greatly appreciate the thoughts and additional comments put forward by Dr. Mishra in regard to our paper. The letter not only addresses proper concerns about our study but also shares some of the following issues and data from a subsequent review undertaken in the literature to provide full disclosure to the reader.

The letter reinforces clearly our findings that cost in thyroid surgery remains a challenging problem for most countries.

Techniques and technologies applied for thyroid surgery as laryngeal examination, intraoperative pathological examination, energy based devices, robotics are important drivers for increased operating and hospitalization costs (1-5).

Loch-Wilkinson TJ *et al.* allured that intraoperative neural monitoring (IONM) can never be cost-effective as measured by true cost per nerve injury prevented, assuming of course that any nerve injury is prevented at all (6). We confirmed that IONM accounts for 5.8–7.2% increase on hospitalization cost, 10–13% on surgery cost, that IONM cost per procedure is sensitive to the volume of activity that is 215.2€ (for 5 thyroidectomies/week) and 272.8€ (1 thyroidectomies/week), and that the cost of Energy based devices cost is higher than IONM (7).

Furthermore, morbidity after thyroid surgery has its economic weight on patient and society (8,9).

In a study, direct and indirect costs in resources consumption management in patients with recurrent

laryngeal nerve (RLN) injury have been estimated (8). Five clinical pathways were identified, based on the result of the RLN injury with vocal fold paralysis: vocal folds function recovery within one, three and six months (first, second and third clinical pathways respectively) and vocal fold permanent paralysis after six months until one year without and with phono-surgery (clinical pathway four and five respectively). Costs were valued from the National Health System (NHS) and patient perspectives (i.e., in terms of productivity losses as human capital approach) (9). Both from NHS and patient perspectives, the analysis showed a significant increase in costs related to the injured patient management (9).

The overall cost-effectiveness of iPTH early measurement has never been reviewed to our knowledge. An attempt to investigate further this analysis to evaluate questions in order to inform clinicians, medical decision making, society and industry will be important in the near future.

The future analysis may demonstrate that the weight of iPTH measurement may be variable depending on the duration, the severity and the prevalence of the parathyroid gland damage, the setting of iPTH use in different countries with sophisticated healthcare economic models, distinct and complex clinical or biochemical decision models, the volume of utilization, type of surgery and indication of surgery potentially allowing tailored treatment strategies, that is identifying patients likely to benefit more from early iPTH measurement. A comparison with other molecules is mandatory too. Moreover, several iPTH properties are difficult to be measured in future study.

For example, prognostication, the intrinsic capacity to predict symptomatic hypocalcemia, quality of life and the intraoperative aid for autotransplantation are iPTH features non measurable.

Cultural, political, economic, and social differences between Countries may limit the generalizability of any study (10-12). Future economic studies, therefore, must be interpreted within the appropriate geopolitical context. De facto, our data presented may be unique and of interest primarily for the Italian Healthcare System: a comparison with systems in other parts of the world is intriguing (13).

In relation to phosphorus matter, we fully agree that the correlation between total calcium and phosphorus values following thyroidectomy have received little importance in literature. The few studies available do not tend to consider the phosphorus (and phosphorus drop) as a predictor of postoperative serum calcium (14) because, probably, of its many confounding factors. Other studies include phosphorus and magnesium as predictors of hypocalcemia; however, their predictive value is significant since the second postoperative day. (15-17).

In our series of patients, we do not have a preoperative phosphorus evaluation neither postoperative, with the exception of patients with renal disease. So we can not correlate phosphorus with iPTH or serum calcium.

It would be useful to have more studies with a larger number of patients to analyze more accurately, the predictive phosphorus value compared to serum calcium.

We agree with Dr. Anand Kumar Mishra and a more careful scrutiny of iPTH clinical effectiveness here presented is definitely required.

Thank you for this opportunity.

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## Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

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