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Thoracic anaesthetic research: 90 years old and still going strong

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Summary:

Ninety years after the first description of one-lung ventilation, the practice of thoracic surgery and anaesthesia continues to develop. Minimally invasive surgical techniques are increasingly being adopted minimising the surgical insult and facilitating improved outcomes. Challenging these outcomes however are parallel changes in patient demographics with more, older and sicker patients undergoing surgery. Thoracic anaesthesia as a speciality continues to respond to these challenges with evolution of practice and a strong academic portfolio.

Narrative:

"*Contemporary thoracic anaesthesia is a culmination of advances in all aspects of anaesthesia*".[1]

Few surgical disciplines have been so dependent for their progress on the development of anaesthetic techniques than the discipline of thoracic surgery. Whist inhalational anaesthesia debuted in the 1840s, it took another 100 years before the combination of the safe provision of one-lung ventilation (OLV) via double lumen endotracheal tubes and routine postoperative pleural drainage set the stage for 'routine' thoracic surgery. Surgical access of the thoracic cavity is now commonplace for cardiac, lung, oesophageal, mediastinal, spinal and vascular procedures. Since the 1990s, the rapid adoption of minimally-invasive thoracic surgery by video-assisted thoracoscopic- or more recently robotic-assisted surgical techniques have led to a paradigm shift in patient experience facilitating enhanced recovery, shortened hospital stay and requiring further thoracic anaesthetic innovation, particularly in terms of analgesia provision. Recent evidence confirming satisfactory oncological outcomes with minimally invasive techniques (one of the main remaining concerns preventing more widespread adoption) means minimally invasive surgery rates are likely to continue to rise.[2]

Whilst by no means the sole indication, much of thoracic surgery and anaesthesia concerns the surgical management of non-small-cell lung cancer. Thankfully, due to public health initiatives and uptake of smoking cessation programmes, lung cancer rates are now waning.[3] However, a broadening of surgical indications, age and fitness criteria for surgical acceptance and earlier diagnosis means that resection rates continue to climb. As a consequence, the thoracic surgical population grows ever older, with a greater burden of comorbidity. Further, in recent years there has been an increasing drive to reduce thresholds of eligibility for acceptable residual predicted postoperative lung function,[4] altogether increasing the challenge for the thoracic anaesthetist. Such a shift in patient demographics drives further focus on patient selection, optimisation, and the merits of prehabilitation and enhanced recovery alongside other techniques which seek to minimise perioperative complications and reduce the burden of postoperative functional limitation and dyspnoea. Indeed, the observed continuing reduction in surgical mortality and complication rates in the face of an increasing patient risk profile must be considered a triumph for the entire multidisciplinary team involved in caring for this challenging surgical population. Looking forward, there is now good evidence that screening programmes seeking to diagnose lung cancer patients at an earlier stage improve mortality. It is believed that widespread implementation of screening programmes currently being rolled out worldwide will, in the UK (for example), result in a 37% increase in surgical resections over the period 2015-2040.[5]

To illustrate the ongoing development of the specialty of thoracic anaesthesia and to showcase the quality of research taking place within the field, the British Journal of Anaesthesia invited submissions for this special issue on 'thoracic anaesthesia and respiratory physiology'. This invitation was timed to coincide with a meeting of the (UK) Association of Cardiothoracic Anaesthesia and Critical Care (held 17-18th November 2021 in Glasgow) which incorporated well-attended thoracic symposia from which several of the published submissions originate. The resulting collection presents a diverse range of articles addressing a wide range of topics. By means of introduction, we shall sign-post to what we believe to be a couple of the thematic highlights of this special edition and hope the BJA readership enjoy reading this collection of articles as much as we have.

Postoperative cardiac function

Two articles in this issue, both involving researchers from the University of Glasgow, address the importance of the heart, specifically right ventricular (RV) function, in patients' outcomes following pulmonary resection.[6, 7] It is fabled that if you take a healthy dog and remove a portion of its lung, then repeat the surgery the next week and keep repeating it week after week, eventually the dog dies of heart failure. Though we hope no one has ever actually tried this, the tale illustrates the perceived importance of cardiac reserve in lung resection patients which remains an under-appreciated and under-investigated subject. In the original investigation by Glass and colleagues,[6] the investigators used cardiovascular magnetic resonance to demonstrates an increase in the reflected pulmonary artery flow waves in patients undergoing lobectomy. This was associated with a decrease of right ventricular function that persisted for 2 months postoperatively (the last testing period). Pulsatile flow resistance is specifically important for the RV and accounts for up to half of its hydraulic work. This investigation is complimented by a review article by Shelley and co-workers[7] which discusses how cardiac dysfunction post-resection contributes to major adverse cardiac effects such as atrial fibrillation, unplanned ICU admissions and decreased long-term functional outcomes.

The thoracic community has become very good at predicting pulmonary mechanical function and gas-exchange capacity post-resection. Predicted post-operative forced expiratory volume in one second (ppoFEV1%) and predicted postoperative carbon monoxide diffusion capacity (ppoDLCO%) are now nearly universally accepted standards.[8] However, whilst our current methods to test preoperative cardio-pulmonary function, such as the preoperative 6-minute walk test[9] or cardiopulmonary exercise testing determination of maximal oxygen consumption, are predictive of overall morbidity and mortality, they remain poor at predicting post-resection cardiac complications, or functional outcomes.[10] Much work remains to be done therefore, to better understand the implications of the observed changes in RV function on patient centered outcomes. In the future, can we develop a valid and specific preoperative RV stress test, or protect the RV perioperatively and so provide a novel therapeutic opportunity? These two articles begin to address this question and open the door for further investigation.

Preventing lung injury and pulmonary complications

Historically, pulmonary complications occurring in patients admitted to the Intensive Care Unit (ICU) and following thoracic surgery were thought to share similar causative mechanisms being triggered by a combination of injurious hits (e. g., surgical or traumatic tissue injuries, sepsis/inflammation, high tidal volume and/or driving pressure, fluid overload, transfusion) causing atelectasis, ventilator-induced lung injury (VILI), pneumonia and acute respiratory distress syndrome (ARDS). Nowadays, with the advent of minimally-invasive thoracic surgery, the neuroendocrine and inflammatory responses are attenuated, the administration of IV fluid is carefully titrated and lung separation with selective ventilation is safely applied with physiological levels of positive end-expiratory pressure (PEEP), low tidal volume and the use of alveolar recruitment manoeuvres (ARM). Yet, despite these seemingly protective interventions, postoperative pulmonary complications (PPCs) continue to be a major issue in the thoracic surgical population with an incidence reported to be as high as 45%[11] and result in prolonged hospital and critical care stay and increased mortality. Unsurprisingly therefore significant research effort continues to be focused on techniques to prevent PPCs. In contrast with thoracic patients undergoing a well-controlled and short-lasting tissue trauma, ICU patients often exhibit one or multiple organ dysfunctions that develop over several days and require prolonged mechanical ventilatory support. Given these differences in patients' phenotype and triggering factors, it perhaps seems logical to explore differences rather than similarities in the pathophysiological

mechanisms of PPCs and to evaluate specific protective pulmonary interventions applicable to each patient population.

In critically-ill patients receiving prolonged mechanical ventilatory support, targeting the lowest driving inspiratory pressure has been associated not only with enhanced oxygenation but also better survival.[12] In this issue, Park and colleagues report a multicentre randomised controlled trial of a similar driving pressure-guided ventilatory strategy compared to conventional ventilation in patients undergoing thoracic surgery.[13] In this study, driving pressure guided OLV does not translate into fewer PPCs despite achieving better respiratory mechanical properties intraoperatively. Such uncoupling between intraoperative physiological effects and postoperative clinical outcome has also been similarly observed in obese patients during abdominal surgery when higher PEEP levels (12 cmH_20) with periodic ARM resulted in more homogenous lung aeration, lower respiratory compliance and enhanced oxygen transport intraoperatively but failed to provide any postoperative clinical benefit compared with lower PEEP (4 cmH_20 and no ARM).[14]

A desire to continue to maintain lung recruitment and avoid atelectasis into the early postoperative period has led to the hypothesis that use of noninvasive ventilation (NIV) following surgery may be an additional prophylactic technique. To this end, in this issue Abrard and co-workers report a multicentre randomized controlled trial of intermittent prophylactic non-invasive ventilation in high risk patients (ARISCAT score >45) undergoing predominantly cardiothoracic surgery.[15] In this study, prophylactic administration of NIV using bilevel positive airway pressure did not reduce the incidence of respiratory failure compared with conventional oxygen inhalation therapy. Though a seemingly disappointing result, this finding is in keeping with the recently reported and analogous 'PRISM' trial, a study of continuous positive airway pressure (rather than NIV) in patients undergoing abdominal surgery.[16] Whilst both studies were challenged by patient tolerance of the intervention, in both, per-protocol analyses demonstrated no significant benefit of the intervention, perhaps suggesting the results reflect a true lack of efficacy rather than simply treatment failure.

Besides attempts to attenuate VILI, muscular weakness associated with poor preoperative physical fitness and postoperative residual effects of anesthetics / neuromuscular blocking agents have been identified as modifiable risk factors for PPCs. In this issue two papers emphasize the benefits of preoperative prehabilitation programs[17] and complete reversal of neuromuscular block.[18] The enhanced physiological reserves achieved with preoperative exercise using respiratory muscle training, whole body endurance training (e.g., biking, running, rowing) or a combination have been shown to be effective to reduce PPCs in cardiac, abdominal and thoracic surgery, even after just one week of preparation.[19] Effective widespread integration of prehabilitation into a modern healthcare settings outwith the controlled environment of a clinical trial however remains a significant challenge. Bradley and colleagues should therefore be commended for their elegant demonstration of the successful implementation of a multicomponent prehabilitation protocol as part of an enhanced recovery after surgery (ERAS) program in 11 UK National Health Service hospitals over an 11-month period.[17] A 12-week exercise program was individualized based on the observed impairment of aerobic fitness and functional capacity. Despite a relatively low participation rate (47%), patient condition improved substantially in terms of walking capacity, perceived health status and quality of life.[17]

In the early postoperative period, greater awareness now surrounds the issue that maximal recovery of muscular function is mandatory to match the increased respiratory work following extubation and to allow early ambulation. In this issue Colqhoun and co-workers report that in a retrospective multicenter cohort study including 3,817 matched pairs, reversal of neuromuscular block at the end of thoracic or abdominal surgery with sugammadex compared with neostigmine was associated with

lower odds of respiratory failure and pneumonia. A meta-analysis of seven cohort studies involving thoracic surgical patients (conducted prior to the publication of the Colqhoun study) further supports this association between sugammadex utilization and fewer PPCs.[20] As the adoption of sugammadex to routine clinical practice gathers pace, the UK National Institute of Health Research has recently funded a large pragmatic clinical trial of "Sugammadex for preventIoN oF pOst-operative pulmoNary complIcAtions (SINFONIA)",[21] to provide further evidence to support practice in addition to addressing concerns concerning the allergy profile of sugammadex.[22]

A challenge unique to the intensive care unit, not found in the provision of mechanical ventilation intraoperatively, is the potential for so-called patient self-inflicted lung injury to contribute to the harmful effects of VILI.[23] In this issue, Wittenstein and colleagues reported similar histopathological changes in alveolo-capillary membrane, inflammatory mediators and diaphragm muscle cells in pigs with ARDS receiving either pressure control ventilation, asynchronous or synchronous pressure assisted ventilation over 12 hours.[24] Interestingly, despite the occurrence of large tidal volumes and transpulmonary pressure swings during asynchronous ventilation, this was not associated with increased VILI in this model of ARDS.

Conclusion

In this editorial, we have provided only a brief summary of the contents of some of this special issue on 'thoracic anaesthesia and respiratory physiology'. This issue contains further excellent investigation and discussion concerning thoracic trauma, spinal anaesthesia, analgesia provision, pulse oximetry and apnoeic oxygenation [*list may need adjusting once final contents of special edition confirmed].* It is heartening to observe the quality of academic endeavor taking place within the field of thoracic anaesthesia and respiratory physiology. Despite it being some 90 years since Gale and Waters published a "preliminary report" describing the first use of OLV for thoracic surgery in 1932,[25] there remains much to learn and we look forward to the further advancement of this branch of clinical and experimental science.

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[Note, many references which pertain to the 'thoracic anaesthesia and respiratory physiology' special edition for which this editorial is an introduction are incomplete and will require to be edited once the edition is typeset].

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