EMA Emergency Medicine Australasia

Emergency Medicine Australasia (2024) **36**, 340–347 doi: 10.1111/1742-6723.14355

ORIGINAL RESEARCH

Does the choice of induction agent in rapid sequence intubation in the emergency department influence the incidence of post-induction hypotension?

Zacchary TAMSETT [1], Ned DOUGLAS [2,3], Cathy KING [1,4], Tanya JOHNSTON [1], Connor BENTLEY [1], Brian HAO [1], Duron PRINSLOO [1] and Elyssia M BOURKE [1,3,5]

[1]Department of Emergency Medicine, Grampians Health, Ballarat, Victoria, Australia, [2]Department of Anaesthesia, The Royal Melbourne Hospital, Melbourne, Victoria, Australia, [3]Department of Critical Care, The University of Melbourne, Melbourne, Victoria, Australia, [4]School of Medicine, Deakin University, Geelong, Victoria, Australia, and [5]Department of Emergency Medicine, The Royal Melbourne Hospital, Melbourne, Victoria, Australia

Abstract

Objective: To describe the effects of different induction agents on the incidence of post-induction hypotension (PIH) and its associated interventions during rapid sequence intubation (RSI) in the ED.

Methods: A single centre retrospective study of patients intubated between 2018 and 2021 was conducted in a regional Australian ED. The impact of induction agent choice, in addition to demographic and clinical factors on the incidence of PIH were determined using descriptive statistics and a multivariate analysis presented as adjusted odds ratios (aORs) and their 95% confidence intervals (CIs).

Results: Ketamine and propofol, used either individually or in conjunction with fentanyl, were significantly associated with PIH (ketamine aOR 4.5, 95% CI 1.35–14.96; propofol aOR 4.88, 95% CI 1.46–16.29). Age >60 years was associated with a greater requirement for vasopressors (aOR 4.46, 95% CI 2.49–7.97) and a higher risk of mortality after RSI (aOR 4.2, 95% CI 1.87–9.40). Patients with a shock index >1.0 were significantly more likely to require vasopressors (aOR 5.13, 95% CI 2.35–11.2) and have a cardiac arrest within 15 min of RSI (aOR 3.56, 95% CI 1.07–11.8).

Conclusions: Exposure to both propofol and ketamine is significantly associated with PIH after RSI, alongside age and shock index. PIH is likely multifactorial in nature, and this data supports the sympatholytic effect of induction agents as the underlying cause of PIH rather than the choice of agent itself. Further prospective work including a randomised controlled trial between induction agents is justified to further clarify this important clinical question.

Key words: *anaesthetic morbidity, induction agents, post-induction hypotension, rapid sequence intubation.*

Key findings

- Exposure to either ketamine or propofol, irrespective of dosing, as well as increasing age and shock index was associated with post-induction hypotension.
- This data does not support the specific induction agent choice as having a significant impact on post-induction hypotension.
- A randomised trial between ketamine and propofol as induction agents for rapid sequence intubation is needed to further explore the association between induction agent choice and post-induction hypotension.

Introduction

Airway management is often undertaken when caring for acutely unwell people in the ED[1] and is usually facilitated using rapid sequence intubation (RSI).[2] RSI is a high-risk procedure with a range of potential complications. The most clinically relevant of these are post-induction hypotension (PIH), oxygen desaturation, unsuccessful or oesophageal intubation, trauma and death.[3,4] PIH is one of the most modifiable complications of RSI. There are numerous risk factors for PIH including increasing age, sepsis, hypovolaemia and cardiac comorbidities.[5,6] PIH is associated with higher in-hospital morbidity and mortality, increased intensive care utilisation and a longer hospital length of stay.[7]

Medication choice is thought to contribute to the development of PIH,

Correspondence: Dr Zacchary Tamsett, Department of Emergency Medicine, Grampians Health, 1 Drummond Street North, Ballarat, VIC 3350, Australia. Email: tzacchary@gmail.com

Zacchary Tamsett, BSc, MD, Emergency Intern; Ned Douglas, MBBS, BMedSci, MSc (Periopmed), MDisast&EmergResp, FANZCA, Consultant Anaesthetist; Cathy King, MD, BHlthSci (Hons), BPharm, Emergency House Medical Officer; Tanya Johnston, MD, Emergency Intern; Connor Bentley, BSc (Hons), Medical Student; Brian Hao, BBiomed, Medical Student; Duron Prinsloo, BBiomedSci (Hons), Medical Student; Elyssia M Bourke, MBBS, BMedSci, MPH, FACEM, Emergency Consultant.

Accepted 14 November 2023

despite limited evidence supporting this hypothesis.[5] Medications used for induction vary between countries based on availability and evidence; however, in Australia the most common agents used are ketamine and propofol, with fentanyl used as a co-induction drug.[4,8] Ketamine is becoming a popular choice due to reports of lower rates of resultant PIH compared to other agents, despite sparse supporting evidence.[9] The literature directly comparing rates of PIH with different induction agents is limited.[9–12] The studies that exist have been undertaken predominantly in metropolitan centres focussing on patients experiencing traumatic injuries, or has been undertaken in non-ED settings,[6,7,13] which may not be representative of all patients being intubated in Australasian EDs.

This study aimed to compare the incidence and severity of PIH across different induction agents used during RSI in a regional Australian ED, as well as clarifying the influence of other risk factors on the likelihood of a patient developing PIH during RSI.

Methods

We performed a retrospective cohort study using standardised chart review of patients who underwent RSI in the Grampians Health Ballarat ED between January 2018 and December 2021 inclusive. This project was approved by the Grampians Health and St John of God Human Research Ethics Committee (LNR/86483/BHSSJOG-2022-328486).

The Grampians Health Ballarat ED cared for 50 920 patients during the 2021 calendar year, of which 1% were Australasian Triage Scale (ATS) category 1, 23% were ATS category 2, 48% were ATS category 3, 25% were ATS category 4 and 2% were ATS category 5 presentations. Approximately 25% of presentations during the study period were of patients aged less than 18 years of age.

An initial review of hospital wide coding data identified 3761 episodes of care where ventilatory support was utilised during the study period. The research team undertook a manual review of these records and removed those involving only non-invasive ventilation, those where the patient was intubated prior to arrival in the ED, and those who were intubated later in their admission.

Medical records at Grampians Health Ballarat are paper-based. Once the patient's episode of care has concluded these forms are scanned into an electronic system where they can be viewed but not edited. Data were extracted from these medical records by the research team using a standardised data-extraction template and data dictionary. Information collected included the triage presenting complaint, indication for RSI, induction agent choice (ketamine, propofol, fentanyl, other) and dosage (mg), muscle relaxant used (rocuronium, suxamethonium, other) and dose (mg), experience level of the intubator (resident, registrar or consultant), specialty background of the intubator (ED, ICU or anaesthesia), vital signs (blood pressure, heart rate, oxygen saturations) immediately prior to RSI and every five min for three recordings following RSI, procedural success (sustained detection of end tidal CO_2 via the endotracheal tube), fluid bolus, vasopressor usage, cardiac arrest within 15 min of the procedure and patient mortality during their admission.

Training was provided to investigators and supervised initial data collection by the lead author occurred before independent data collection. Ten percent of cases were checked by the lead author to ensure accuracy and consensus between authors.

Inclusion criteria

The study included patients aged 18 years and older who underwent RSI in the ED during the study period who had a medical record available for review including details of the procedure, medications provided and vital signs.

Exclusion criteria

The study excluded patients who were intubated before arriving in ED by paramedics, those who were intubated without medications and those who were in cardiac arrest at the time of intubation.

Outcomes

The primary outcome was a composite definition of PIH, defined as any of the following within 15 min of intubation:

1. A systolic blood pressure (SBP) <100 mmHg, or
2. A mean arterial pressure of less than 70 mmHg, or
3. Reduction in mean arterial pressure of more than 20%.

There is limited evidence currently regarding the best outcomes to measure in ED intubation studies to detect potential patient harm. Anaesthetic literature examining this question has provided a consensus that the blood pressure cut-offs outlined above are the most inclusive in detecting patient harm and are therefore the most appropriate to use in further studies.[13,14] Until ED specific literature becomes available, the research team have chosen to utilise these consensus-based outcome measures.

The secondary outcomes for the present study included the percentage reduction of SBP within 15 min of RSI, fluid bolus requirement within 15 min of RSI, vasopressor requirement within the first 15 min of RSI, cardiac arrest within 15 min of RSI, procedural success, and patient mortality during the admission.

Statistical analysis

As prior estimates of effect size were not available, a convenience sample of 4 years worth of data was used and point estimates of the outcomes along with 95% confidence intervals (CIs) are reported. The analysis was performed in Stata 17 (StataCorp, College Station, TX, USA).

For the primary outcome, a descriptive statistics and multivariate logistic regression analysis was conducted. After reviewing the univariate associations between each factor (age as a continuous variable, age >60 years, ketamine exposure, propofol exposure, fentanyl exposure,

muscle relaxant [suxamethonium *vs* rocuronium], multiple intubation attempts, shock index as a continuous variable, shock index >1.0, SBP prior to induction, mean arterial pressure prior to induction, heart rate prior to induction, indication for intubation class) and PIH, a purposeful selection approach was undertaken to construct the most parsimonious model with the maximum possible explanatory power. Selection for subsequent inclusion required a clinically realistic link between the exposure and hypotension, in addition to a *P*-value less than 0.2 in the multivariate model. Investigation of alternative classification schemes for continuous variables with a large scale (age, shock index, oxygen saturations prior to induction) was conducted before model optimisation. Indications for intubation were observed to be widely variable and were classified by the investigators before model construction began to ensure that patients with similar pathological disturbances were classed together, acknowledging that multiple pathologies could exist in the same patients. For the final model, variables were thought to be associated with the primary outcome if the *P*-value associated with the variable was less than 0.05. To understand the utility of these predictive variables for the secondary outcomes, the existing variables from the final multivariate model of the primary outcome were used to construct multivariate models for each secondary outcome in turn.

Further details regarding the creation of the model can be found in Supporting Information.

Results

There were 3761 unique patients reported as requiring ventilatory support during their hospital stay throughout the study period. These records were reviewed and filtered based on their fulfilment of the inclusion criteria summarised in Figure 1. Of those assessed for eligibility, 266 met the criteria for inclusion in the present study. One hundred and sixty male patients were included with the remaining 106 listed as female.

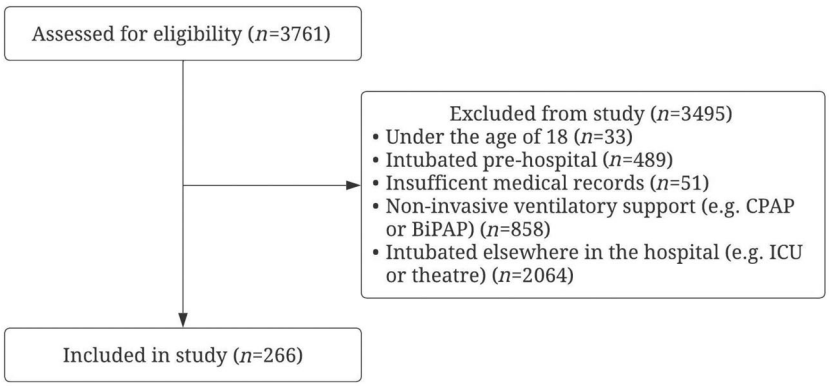

Figure 1. *CONSORT diagram of the patient search and inclusion.*

The patients were triaged as category 1 ($n = 132$, 49.6%), category 2 ($n = 103$, 38.7%), category 3 ($n = 29$, 10.9%) and category 4 ($n = 2$, 0.8%).

The presentation variables and haemodynamics of patients are presented in Table S1. For the primary outcome, 63 (54%) of 117 patients exposed to ketamine alone became hypotensive, whereas 69 (52%) of 132 patients exposed to propofol alone became hypotensive, 7 (58%) of 12 patients exposed to both ketamine and propofol became hypotensive and 0 (0%) of 5 patients exposed to thiopentone became hypotensive.

The majority (87%) were intubated by emergency medicine specialists, with intensive care and anaesthetic doctors involved in the minority of cases (13%). Experience levels of the proceduralists varied, with 54% being consultants, 41% being registrars and the remaining not able to be identified accurately. First pass success for all patients was 90%. The indications for intubation are summarised in Figure 2, and the primary patient presenting concern in Figure S1.

A total of 35% of inductions required vasopressors within 15 min due to haemodynamic instability.

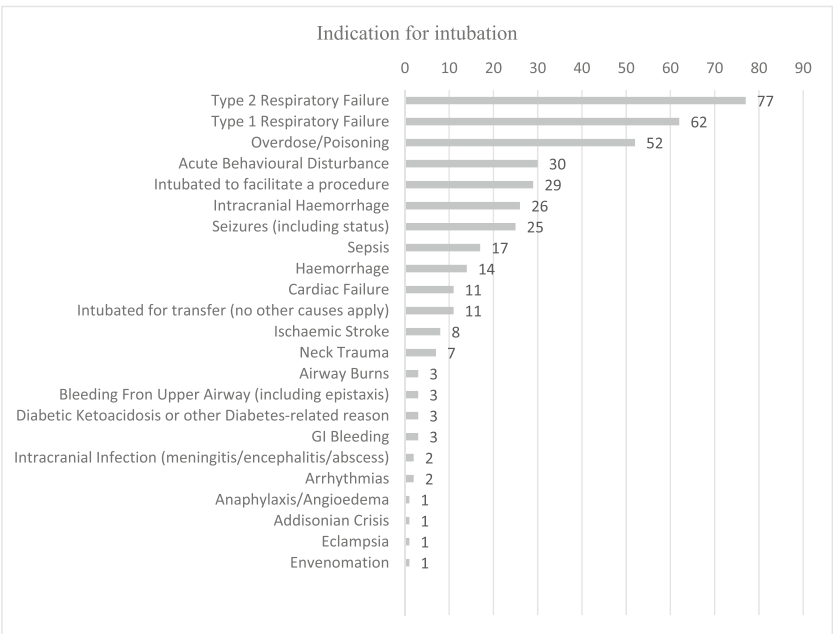

Figure 2. *Indication for intubation. More than one indications for intubation can be selected for each patient to account for the complexity of some clinical scenarios.*

TABLE 1. *Haemodynamic changes and outcomes of intubation attempts*

	Overall $n = 266$	Ketamine induction $n = 117$ (44%)	Propofol induction $n = 132$ (50%)	Both agents used $n = 12$ (5%)	Thiopentone $n = 5$ (2%)
Haemodynamics of patients prior to and 5-, 10- and 15-min post induction					
Heart rate prior to induction (mean)	98	102	93	115	99
Systolic blood pressure (SBP) prior to induction (mean)	135	127	141	144	141
Oxygen saturations prior to induction (mean)	97	97	98	96	99
Heart rate 5 min post induction (mean)	102	105	97	121	117
SBP 5 min post induction (mean)	127	125	127	127	154
Oxygen saturations 5 min post induction (mean)	98	98	98	97	98
Heart rate 10 min post induction (mean)	101	105	96	113	113
SBP 10 min post induction (mean)	124	120	126	124	158
Oxygen saturations 10 min post induction (mean)	99	98	99	98	99
Heart rate 15 min post induction (mean)	98	102	93	111	109
SBP 15 min post induction (mean)	123	119	126	117	164
Oxygen saturations 15 min post induction (mean)	99	99	99	98	99
Progress and outcomes of the intubation					
Procedural success (defined as sustained end tidal CO_2 trace) (*n*, %)	266 (100)	117 (100)	132 (100)	12 (100)	5 (100)
First pass success (*n*, %)	240 (90)	105 (90)	119 (90)	11 (92)	5 (100)
Requirement for a fluid bolus	45 (17)	21 (18)	21 (16)	3 (25)	0
Requirement for vasopressor medications (*n*, %)					
Overall	93 (35)	46 (39)	42 (32)	4 (33)	1 (20)
Adrenaline	11 (4)	6 (5)	5 (4)	0	0
Noradrenaline	5 (2)	3 (3)	2 (2)	0	0
Metaraminol	55 (21)	18 (15)	33 (25)	3 (25)	1 (20)
Multiple agents	22 (8)	19 (16)	2 (2)	1 (8)	0
Cardiac arrest (*n*, %)	13 (5)	8 (7)	5 (4)	0	0
ED and in-hospital mortality (*n*, %)	37 (14)	24 (20)	13 (10)	0	0

Hospital mortality during the index admission was 14%. Full details of the haemodynamic changes and secondary outcomes are contained in Table 1.

Univariate associations between potentially predictive variables and the primary outcome were assessed using logistic regression. Odds ratios (ORs) and CIs are displayed in Table S2.

Multivariate logistic regression using purposeful selection was then conducted. The final model was significant ($\chi^2 = 32.64$, $P < 0.0001$) (Table 2), and revealed independent associations between both propofol (adjusted OR [aOR] 4.88, 95% CI 1.46–16.29, $P < 0.01$) and ketamine exposure (aOR 4.5, 95% CI 1.35–14.96, $P = 0.014$) and PIH. Fentanyl exposure was not associated with PIH (aOR 1.51, 95% CI 0.87–2.63, $P = 0.14$). Age >60 years was associated with PIH (aOR 2.9, 95% CI 1.69–5.02, $P < 0.001$) as was a shock index >1.0 (aOR 3.05, 95% CI 1.4–6.64, $P = 0.005$). Indication for intubation was not included in the final model as there was no association between any individual category and the primary outcome. Choice of muscle relaxant was not significantly associated with the risk of PIH (*P*-value for suxamethonium as opposed to rocuronium = 0.44). The area under the receiver operating characteristic curve for the final model was 68%.

TABLE 2. *Final multivariate logistic regression model details for hypotension within 15 min post induction*

Exposure variable	aOR	95% confidence interval	*Z*	*P*-value
Age >60 years	2.9	1.69–5.02	3.85	<0.001
Ketamine exposure	4.5	1.35–14.96	2.45	0.014
Propofol exposure	4.88	1.46–16.29	2.58	0.01
Fentanyl exposure	1.51	0.87–2.63	1.48	0.14
Shock index >1.0	3.05	1.4–6.64	2.81	0.005

The secondary outcomes were examined using multiple logistic regression. None of the included variables (Table 3) were significantly associated with increased odds of administration of a fluid bolus in the first 15 min after induction. Age >60 years (OR 4.46, 95% CI 2.49–7.97, $P < 0.001$) and a shock index >1.0 (OR 5.13, 95% CI 2.35–11.2, $P < 0.001$) were significantly associated with the requirement for vasopressors within 15 min following induction. A shock index of >1.0 was positively associated with those experiencing cardiac arrest in the 15 min following induction (OR 3.56, 95% CI 1.07–11.8, $P = 0.038$) although the overall rates of cardiac arrest in the study population were low with only 13 (5%) total events. Age 60 years or greater was associated with an increased rate of in-hospital mortality (OR 4.2, 95% CI 1.87–9.40, $P = 0.001$). The absolute dose of ketamine ($P < 0.46$), propofol ($P < 0.911$) and fentanyl ($P < 0.235$) were not significantly predictive of the percentage reduction in SBP.

TABLE 3. *Multivariate logistic regression model details for all secondary outcomes*

Exposure variable	aOR	95% confidence interval	*Z*	*P*-value
Administration of a fluid bolus within 15 min post induction				
Age >60 years	1.36	0.69–2.69	0.88	0.378
Ketamine exposure	1.94	0.55–6.9	1.03	0.305
Propofol exposure	2.27	0.61–7.7	1.19	0.234
Fentanyl exposure	0.58	0.28–1.22	−1.43	0.15
Shock index >1.0	2.15	0.97–4.8	1.87	0.061
Administration of vasopressors within 15 min post induction				
Age >60 years	4.46	2.49–7.97	5.05	<0.001
Ketamine exposure	1.23	0.64–7.01	1.23	0.217
Propofol exposure	1.86	0.56–6.12	1.02	0.308
Fentanyl exposure	1.65	0.91–3.00	1.65	0.1
Shock index >1.0	5.13	2.35–11.2	4.12	<0.001
Cardiac arrest within 15 min post induction				
Age >60 years	1.75	0.55–5.6	0.94	0.346
Ketamine exposure	0.79	0.047–12.9	−0.17	0.866
Propofol exposure	0.53	0.03–8.6	−0.46	0.652
Fentanyl exposure	1.02	0.3–3.43	2.08	0.971
Shock index >1.0	3.56	1.07–11.8	4.12	0.038
In-hospital mortality				
Age >60 years	4.2	1.87–9.40	3.49	0.001
Ketamine exposure	1.13	0.17–7.55	0.13	0.895
Propofol exposure	0.62	0.09–4.05	−0.5	0.615
Fentanyl exposure	1.47	0.67–3.24	0.96	0.338
Shock index >1.0	1.67	0.66–4.29	1.1	0.27

Discussion

The present study is the first to examine factors associated with PIH in a regional mixed ED. Our study is significant in that it found that both ketamine and propofol were significantly associated with PIH, but there was no clinically significant difference between these agents regarding the rates of PIH. This aligns with previous literature that suggests that participant factors such as age, baseline mean arterial pressure and shock index, rather than the induction agent used, are the most important predictors of PIH in emergency intubation.[15,16]

Our study is the first to simultaneously examine the association between ketamine and propofol and the risk of PIH in an ED, and is consistent with the idea that exposure to either agent poses a significant risk of developing PIH. The similarity of both the strength of the association and the size of the effect between the induction agents suggests that the induction of anaesthesia with associated sympatholysis, reduction in systemic vascular resistance, and decreased plasma catecholamine concentrations are the driving force behind PIH rather than the pharmacodynamics of the specific agents chosen.[10,11,17–19] Previous literature has found no association between

higher and lower dosing of ketamine or propofol in PIH,[20,21] which was also observed in the present study. The present study adds to existing evidence that ketamine does not guarantee that a patient will avoid hypotension when shocked at the time of intubation.[5,22]

Our study found that the use of vasopressors within the acute period post induction was associated with an age >60 years and with a shock index >1.0, which is consistent with previous literature.[6,23] Anticipation of PIH in shocked patients and establishing intubation protocols that prepare clinicians for the increased likelihood of vasopressor requirements based on patient age and shock index could be incorporated into ED intubation guidelines to ensure patient safety is maintained as haemodynamic instability in the immediate post-intubation period is associated with higher in-hospital and 90-day mortality.[24] Cardiac arrest was also identified in our study to occur more frequently in those patients with a shock index >1.0 before intubation. Optimisation of all patients' haemodynamic status prior to intubation through the use of intravenous fluid boluses and/or vasopressor medications may reduce the risk of cardiac arrest.[25] Mortality following RSI in our study was found to be associated with an age >60 years or a shock index >1.0, which is consistent with current literature.[23,26]

The consistent association of shock index and older age with the risk of PIH, need for vasopressor administration, cardiac arrest and mortality suggests these are important factors in explaining physiological deterioration after intubation, and this data reinforces the idea that pre-procedural optimisation is key to improving outcomes.[27,28] These outcomes may be determined by many factors that may not have been measured in the present study, such as a limited physiological ability to respond to acute stress, poor baseline cardiovascular function and underlying degenerative neurological changes.[29,30] To confirm these findings, a large randomised controlled trial is required to clarify if a real difference in patient centred outcomes does in fact exist.

Limitations

Definitive findings using this data are limited. The retrospective nature of the study means confounding by indication, and the influence of unmeasured variation not explained by the captured variables is potentially significant. The authors were unable to establish the relative timings of the medications provided, or to determine individual clinician decision making regarding the use of medications as a pre-treatment or part of the RSI, or the delineate the choice to use a particular induction agent based on patient factors due to the retrospective nature of the data. Furthermore, as patient weight was not well recorded, determining a mg/kg dosing regimen for patients was not possible in the present study.

All information collected required manual extraction from a paper-based medical record, meaning data points chosen for extraction were judicious. As a result, some potentially useful variables were not measured, including whether or not patients received vasopressors prior to induction.

Furthermore, 16% of patients lacking critical information relating to the primary outcome in the medical record resulted in their exclusion from the study. The smaller size of the sample means that the uncertainty of the effect sizes is large, and the study is likely to be underpowered for the rarer secondary outcomes, particularly in relation to cardiac arrest and hospital mortality.

The present study draws on data obtained during the COVID-19 pandemic, where changes to patient management introduced in the name of staff safety may have affected several of the measured outcomes.

Patients in the ketamine group had a lower pre-induction blood pressure than those in the propofol group. Although the use of the shock index and the regression analysis were used to control for these factors, it is difficult in a retrospective study to definitely determine if there was a difference between the groups receiving each induction agent which could have potentially influenced their response to each induction agent.

Conclusion

Post-induction hypotension was associated with both ketamine and propofol exposure, alongside increasing age and shock index in this regional ED cohort. This data does not support the specific induction agent choice as having a significant influence on the risk of PIH in this patient population. The choice of induction agent was not associated with clinically important secondary outcomes. Acknowledging the limitations of this retrospective cohort study, a randomised trial between ketamine and propofol as induction agents for emergency intubation is the next step in exploring the association between induction agent choice and these clinically relevant outcomes to remove confounding bias on induction agent choices.

Author contributions

ZT, ND and EMB contributed to the study design and ethics approval. All authors were involved with data collection and auditing. ZT, ND and EMB were involved in the statistical analysis of the data. All authors were involved in the drafting of the manuscript. All authors have approved the final submitted manuscript.

Competing interests

None declared.

Data availability statement

The data that support the findings of this study are available on reasonable request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

References

1. Soar J, Nolan JP, Böttiger BW *et al*. European resuscitation council guidelines for resuscitation 2015: section 3. Adult advanced life support. *Resuscitation* 2015; **95**: 100–47.
2. Alkhouri H, Vassiliadis J, Murray M *et al*. Emergency airway management in Australian and New Zealand emergency departments: a multicentre descriptive study of 3710 emergency intubations. *Emerg. Med. Australas.* 2017; **29**: 499–508.
3. Mace SE. Challenges and advances in intubation: rapid sequence intubation. *Emerg. Med. Clin. North Am.* 2008; **26**: 1043–68.
4. Phillips L, Orford N, Ragg M. Prospective observational study of emergent endotracheal intubation practice in the intensive care unit and emergency department of an Australian regional tertiary hospital. *Emerg. Med. Australas.* 2014; **26**: 368–75.
5. Groth CM, Acquisto NM, Khadem T. Current practices and safety of medication use during rapid sequence intubation. *J. Crit. Care* 2018; **45**: 65–70.
6. Smischney NJ, Kashyap R, Khanna AK *et al*. Risk factors for and prediction of post-intubation hypotension in critically ill adults: a multicenter prospective cohort study. *PLoS One* 2020; **15**: e0233852.
7. Heffner AC, Swords D, Kline JA, Jones AE. The frequency and significance of postintubation hypotension during emergency airway management. *J. Crit. Care* 2012; **27**: 417.e9–e13.
8. Freeman J, Alkhouri H, Knipp R, Fogg T, Gillett M. Mapping haemodynamic changes with rapid sequence induction agents in the emergency department. *Emerg. Med. Australas.* 2022; **34**: 237–43.
9. Ferguson I, Alkhouri H, Fogg T, Aneman A. Ketamine use for rapid sequence intubation in Australian and New Zealand emergency departments from 2010 to 2015: a registry study. *Emerg. Med. Australas.* 2019; **31**: 205–10.
10. Baradari AG, Alipour A, Habibi MR, Rashidaei S, Emami ZA. A randomized clinical trial comparing hemodynamic responses to ketamine-propofol combination (ketofol) versus etomidate during anesthesia induction in patients with left ventricular dysfunction undergoing coronary artery bypass graft surgery. *Arch. Med. Sci.* 2017; **13**: 1102–10.
11. Soleimani A, Heidari N, Habibi MR *et al*. Comparing hemodynamic responses to diazepam, propofol and etomidate during anesthesia induction in patients with left ventricular dysfunction undergoing coronary artery bypass graft surgery: a double-blind, randomized clinical trial. *Med. Arch.* 2017; **71**: 198–203.
12. Ferguson I, Buttfield A, Burns B *et al*. Fentanyl versus placebo with ketamine and rocuronium for patients undergoing rapid sequence intubation in the emergency department: the FAKT study—a randomized clinical trial. *Acad. Emerg. Med.* 2022; **29**: 719–28.
13. Südfeld S, Brechnitz S, Wagner JY *et al*. Post-induction hypotension and early intraoperative hypotension associated with general anaesthesia. *Br. J. Anaesth.* 2017; **119**: 57–64.
14. Sessler DI, Bloomstone JA, Aronson S *et al*. Perioperative quality initiative consensus statement on intraoperative blood pressure, risk and outcomes for elective surgery. *Br. J. Anaesth.* 2019; **122**: 563–74.
15. Jor O, Maca J, Koutna J *et al*. Hypotension after induction of general anesthesia: occurrence, risk factors, and therapy. A prospective multicentre observational study. *J. Anesth.* 2018; **32**: 673–80.
16. Chen B, Pang QY, An R, Liu HL. A systematic review of risk factors for postinduction hypotension in surgical patients undergoing general anesthesia. *Eur. Rev. Med. Pharmacol. Sci.* 2021; **25**: 7044–50.
17. Saugel B, Bebert EJ, Briesenick L *et al*. Mechanisms contributing to hypotension after anesthetic induction with sufentanil, propofol, and rocuronium: a prospective observational study. *J. Clin. Monit. Comput.* 2022; **36**: 341–7.
18. Basagan-Mogol E, Goren S, Korfali G, Turker G, Kaya FN. Induction of anesthesia in coronary artery bypass graft surgery: the hemodynamic and analgesic effects of ketamine. *Clinics (Sao Paulo)* 2010; **65**: 133–8.
19. Hoffman WE, Pelligrino D, Werner C, Kochs E, Albrecht RF, Schulte am Esch J. Ketamine decreases plasma catecholamines and improves outcome from incomplete cerebral ischemia in rats. *Anesthesiology* 1992; **76**: 755–62.
20. Driver BE, Trent SA, Prekker ME, Reardon RF, Brown CA 3rd. Sedative dose for rapid sequence intubation and postintubation hypotension: is there an association? *Ann. Emerg. Med.* 2023; **82**: 417–24.
21. Sjøen GH, Falk RS, Hauge TH, Tønnessen TI, Langesæter E. Hemodynamic effects of a low versus a high dose of propofol during induction of anesthesia. A randomized trial. *Acta Anaesthesiol. Scand.* 2023; **67**: 1178–86.
22. Miller M, Kruit N, Heldreich C *et al*. Hemodynamic response after rapid sequence induction with ketamine in out-of-hospital patients at risk of shock as defined by the shock index. *Ann. Emerg. Med.* 2016; **68**: 181–8.e2.
23. Trivedi S, Demirci O, Arteaga G, Kashyap R, Smischney NJ. Evaluation of preintubation shock index and modified shock index as predictors of postintubation hypotension and other short-term outcomes. *J. Crit. Care* 2015; **30**: 861–7.
24. Smischney NJ, Demirci O, Ricter BD *et al*. Vasopressor use as a surrogate for post-intubation hemodynamic instability is associated with in-hospital and 90-day mortality: a retrospective cohort study. *BMC. Res. Notes* 2015; **8**: 445.
25. De Jong A, Rolle A, Molinari N *et al*. Cardiac arrest and mortality related to intubation procedure in critically ill adult patients: a multicenter cohort study. *Crit. Care Med.* 2018; **46**: 532–9.
26. Ouchi K, Jambaulikar GD, Hohmann S *et al*. Prognosis after

emergency department intubation to inform shared decision-making. *J. Am. Geriatr. Soc.* 2018; **66**: 1377–81.
27. Olaussen A, Blackburn T, Mitra B, Fitzgerald M. Review article: shock index for prediction of critical bleeding post-trauma: a systematic review. *Emerg. Med. Australas.* 2014; **26**: 223–8.
28. Kurt E, Bahadirli S. The usefulness of shock index and modified shock index in predicting the outcome of COVID-19 patients. *Disaster Med. Public Health Prep.* 2022; **16**: 1558–63.
29. Strøm C, Rasmussen LS, Sieber FE. Should general anaesthesia be avoided in the elderly? *Anaesthesia* 2014; **69**: 35–44.
30. Van Dijck CP, Vanelderen P, Van Boxstael S. Ketamine for emergency endotracheal intubation: insights into post-induction hemodynamic instability. *Intensive Care Med.* 2022; **48**: 778.

Supporting information

Additional supporting information may be found in the online version of this article at the publisher's web site:

Table S1. Presentation variables, haemodynamics and outcomes of participants intubated in the ED during the study period.
Table S2. Univariate associations between exposure variables of potential interest and the primary outcome.
Figure S1. Primary presenting complaint. The presenting triage complaint was the one recorded by the triage practitioner at the ED as the principal cause for presentation.