Degree Project in medicine

By Nick Lindholm

Postoperative Delirium & use of

Dexmedetomidine vs. Propofol

A clinical randomized controlled trial

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Abstract

Introduction: Postoperative delirium (POD) is a complication with severely negative prognostic effects on elderly patients with acute hip fracture (AHF). Dexmedetomidine is used for sedation and treatment of delirium in the intensive care unit (ICU). We intended to study its effects on POD when used for sedation in AHF surgery when compared to Propofol.

Method: AHF patients were included prior to surgery after patient approval and randomized into two groups: Dexmedetomidine or Propofol. In the two days following surgery, patients were assessed with the Confusion Assessment Method for ICU (CAM-ICU) questionnaire once daily, and dosages of fast-acting opioids were converted into morphine-equivalent units these 48 hours. Intraoperative pCO2 values were collected from anesthesia journals.

Results: Incidence of POD was 18.2% in the Dexmedetomidine group, and 26.7% in the Propofol group. Average length of hospital stay (LOS), 48 hour opioid use, and intraoperative pCO2 differed negligibly between the two groups.

Discussion: While our study has limitations especially regarding statistical significance and ability to generalize the results, Dexmedetomidine warrants further study in larger trials.

Introduction

Postoperative delirium (POD) constitutes a major problem in the care of elderly patients with acute hip fracture (AHF).[1] Aside from the emotional impact of a delirious episode in patients and relatives, patients who develop the condition following surgery also have an increased 15-, 30- and 90-day mortality and extended length of hospital stay (LOS).[2]

Delirium

Delirium is a condition with a multi-factorial etiology that especially manifests in the elderly. The Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-V) defines delirium as a state of disturbed attention, cognition and consciousness with a fluctuating course. The deficits often manifest as communicative issues , as the affected individual often does not understand or perceive a question or command. Auditory, visual and sensory hallucinations are also phenomena of delirium.[3] Delirium can be both acute, lasting for approximately 7 days, and chronic, lasting for weeks to months.[4] Furthermore, long-lasting cognitive deficits and/or decline has been shown to follow delirious episodes. As one would understand, this is especially a problem for elderly patients who might suffer from dementia and other forms of cognitive impairment.

The DSM-V further categorizes delirium differently depending on the symptoms – hyperactive delirium, characterized by arousal and agitation; hypoactive, which is more catatonic in nature; and mixed forms with elements of both of the aforementioned two states.[5] While hyperactive delirium is fairly easy for an observing health care provider to recognize, the other forms are more insidious as they might be missed and left un-

diagnosed and not receive treatment, causing the patient unnecessary suffering and complicating care.[6]

These forms of delirium all result in problems and difficulties with the care of frail, sick or elderly patients, as the patient might not be capable of cooperating with being moved, receiving treatment or being examined. As one might infer, this also means that hospital-acquired injuries and sicknesses can be more difficult to prevent in a patient suffering from delirium. Length of hospital stay is often extended, both due to the delirium requiring extra treatment with medication that require physician-observed weaning, and the risk of further injuries and sicknesses and the treatment of those. The patients recovering from delirious episodes often report traumatic experiences, and depression and post-traumatic stress disorders as sequelae from delirium are not uncommon. Therefore, it is of utmost importance for hospital personnel and care providers to be vigilant in both recognizing and preventing the development of delirium.

Risk factors for delirium include dementia, older age, co-morbid illness, severity of illness, infection, high risk medication use (such as opioids, sedatives and anesthetics), diminished activities of daily living, immobility, sensory impairment, urinary catheterization, urea and electrolyte imbalance and malnutrition.[7] As one might imagine from these risk factors, an elderly patient with an acute hip fracture is a very high risk individual for developing delirium, especially following surgical treatment.

The elderly patient

Sweden has a large elderly population. The percentage of people >65 years of age is approximately 20%,[8] and that number is expected to grow further in the coming decades, as the average life expectancy is increasing. Likewise, the older population is becoming more and more physically active, which is reflected in an increasing demand for senior gymnastics classes and outdoor activities for pensioners. A risk when conducting physical activity is often fall trauma, and acute traumatic hip fracture is a common injury in the elderly. Acute hip fracture is a serious injury, especially in a geriatric patient – aside from the injury itself and convalescence time following treatment, there is a 38% risk of death within two years, and 3% during hospital stay.[9]

Dexmedetomidine

Dexmedetomidine is a selective α2-receptor agonist with sympatholytic and sedative properties that has previously been successfully used for sedation and treatment of delirium in intensive care units across Swedish hospitals.[10] Its mechanism of action is that it, suppresses norepinephrine transmission in sympathetic nerve endings and in the brainstem, achieving sedation. It also has a much lower clinical risk of respiratory depression in comparison to Propofol and other common sedatives, in part owing to its analgesic properties decreasing use of opioid medication. Dexmedetomidine's indication in Sweden has recently been broadened to include surgical sedation, but there is scarce previous data on its efficiency in preventing POD after surgery with spinal anesthesia combined with sedation, at least when compared to other sedative agents, such as Propofol.

However, there are promising findings seen in studies conducted by other authors. In 2018, a systematic review and meta-analysis by Duan et al, encompassing eighteen studies and 3309 patients, concluded that Dexmedetomidine can reduce POD incidence in adult cardiac and non-cardiac surgical patients. Trial sequential analysis showed that there was a firm reduction in risk of POD across the entire adult surgical population with an odds ratio of 0.35 (95% Confidence Interval 0.25-0.51). However, the article also stressed that evidence for secondary outcome measurements such as in-hospital mortality and hospital length of hospital stay was thus far insufficient for any conclusions to be drawn.[11]

Another meta-analysis by Wu, Liang, Dai and Wang examined the results of ten randomized controlled trials comparing the effect of perioperative treatment with Dexmedetomidine versus non-treatment (normal saline, propofol and other anesthetic drugs) for cardiac surgery, finding a significant decrease in incidence of POD. In-hospital length did not differ significantly between Dexmedetomidine and non-treatment in these studies.[12]

Propofol

Propofol was the substance we decided to use for sedation in the control group, due to it having a decades long history of use for anesthesia and sedation in hospital systems across the world, and still remaining the gold standard in Swedish hospitals. Its popularity is owed to its low risk profile, rapid induction and recovery time compared to other sedatives.[13] The mechanism of action of Propofol is not fully understood, and is proposed to work in multiple ways, both as a $GABA_A$ receptor positive allosteric modulator and a direct $GABA_A$ receptor agonist.[14]

Study purpose and outcome measurements

The major aim of this clinical trial was to investigate the effects of Dexmedetomidine on the incidence of POD, and compare with Propofol. Secondary parameters were length of hospital stay and 30-day mortality, as, while these outcomes have been explored previously, there still is not enough data to draw a conclusion on whether Dexmedetomidine improves, worsens or has similar effects as Propofol on those outcomes. Lastly, following preliminary results, we included intra-operative pCO2 values, and the total 48 hour dosages of fast-acting opioids as tertiary measurements.

Research Aim

To assess the effects of Dexmedetomidine on the incidence of POD and post-operative recovery and survival.

Method and study design

Patients > 65 years with AHF were included when scheduled for surgery at Sahlgrenska University Hospital, Mölndal, Sweden over a period starting in September 2019 and ending in April 2020.

Inclusion and exclusion criteria are outlined in the table below.

Criteria for inclusion	Criteria for exclusion
Patient with AHF planned for surgery within 24 hours of admission to hospital	Malignancy-associated fractures
Patient in geriatric or orthopedic care units	Distal femur fractures (distal of trochanter minor)
Age >65 years	Age <65 years
Patient planned for spinal anesthesia with sedation	Patient planned for general anesthesia
	Kidney failure with S-Creatinine >200
Patient with Short portable mental status questionnaire (SPMSQ) >7 (Cognitively intact)	Patient with SPMSQ <7 (cognitive impairment, dementia)
Normal CAM-ICU at admission and preoperative care (e. g. no incidence of preoperative delirium)	Pathological CAM-ICU i.e. preoperative delirium
Patient consenting to participate in the study following verbal and written information	Patient declining to participate

	Patient with alcohol use disorder or impaired liver function
	Previous participant of this study

Patients were preoperatively assessed in their respective clinics: units 234 & 235, geriatric care, and unit 232, orthopedic care. Following verbal and written study information, patients gave written consent to participate.

Following inclusion, patients were randomized into one of two groups: Dexmedetomidine (D) or Propofol (P). Randomization was single-blinded and performed by opening the topmost envelope in a shuffled stack of envelopes, containing a note with either 'P' or 'D'. This also means that the while the patients were not aware of what medication they would receive, the researchers were.

Blood samples were drawn to assess the patients' Hemoglobin, Creatinine and Albumin. Patients' SPMSQ scores, prevalence of systemic disease, and prescribed medication were obtained from hospital journal documentation.

Patients randomized to the Dexmedetomidine group received a continuous intravenous infusion of 0.2-0.3 µg/kg/h. Meanwhile, patients in the Propofol group were induced with 1-2 mg/kg of Propofol, followed by a continuous intravenous infusion with 2-4 mg/kg/h.

During surgery, all patients in both groups were monitored with bi-spectral analysis (BIS) to assess level of sedation. Intraoperatively, arterial blood gases (ABG) were taken 2-3 times to measure peripheral carbon dioxide (pCO2) levels. In the 48 hours following surgery, patients were assessed daily by a senior researcher and anesthesiologist or a 5th year

medical student with the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) questionnaire to diagnose POD.

CAM-ICU includes tests of:

Acute change or Fluctuating course of mental status	- From baseline OR - In the past 24 hours
Inattention	
Altered level of consciousness	Current Richmond Agitation-Sedation Scale (RASS) level
Disorganized thinking	

For a more comprehensive explanation, please see appendix 1. Furthermore, due to the fluctuating nature of delirium as a condition, we have also decided to include a “clinical” diagnosis of delirium, acquired by conversation with ward nurses and reading their daily journal on the study participants, so as not to miss any patient developing delirium following surgery.

Each daily assessment of POD was noted in an excel spreadsheet, along with other data as outlined above. If a patient either tested positive for delirium by CAM-ICU or by “clinical” diagnosis, they were considered to have delirium for the rest of the 48 hour post-operative period, *i.e*. the same patient could not be noted to develop delirium twice. Administration of opioids outside of the routine ordinations for post-operative care of AHF was converted into morphine-equivalent doses, and entered into the spreadsheet. In all other aspects, treatment and care of participants were identical to that of non-participants.

Following collection of data, statistical analysis was conducted with Fisher's exact test and further verified with a binomial proportion test using significance levels of 0.05 and 0.1.

Ethics

The study was approved by the National Ethics Committee (2019-03371). Recruitment occurred prior to surgery and the patients received both oral and written study information. Following informed consent, randomization to Dexmedetomidine or Propofol was performed.

Results

We recruited a total of 69 patients during the study period. Recruitment was prematurely halted due to the COVID-19 pandemic. Some patients were excluded according to the exclusion criteria outlined above. Following exclusions, a total of 52 patients remained. Out of those 52, 30 received Propofol and 22 received Dexmedetomidine.

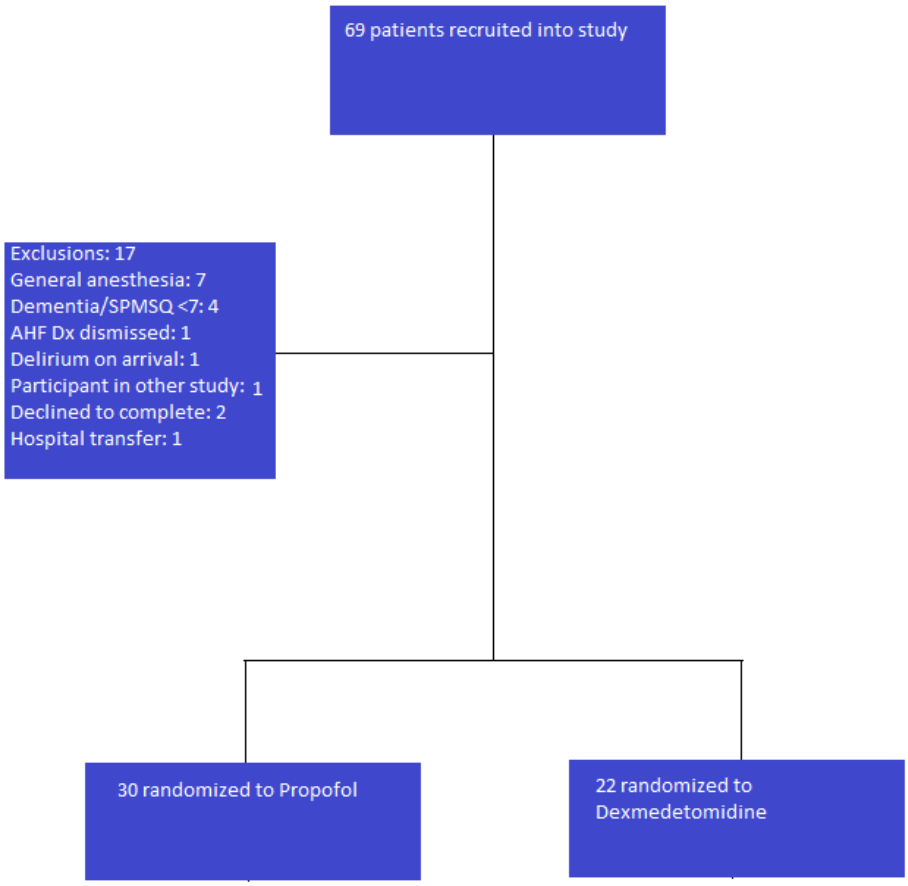

Fig. 1. Consort diagram of patients recruited, exclusions and number of participants per group.

The Propofol group of patients was younger, with an average age of 80.3 (70-94) years, while the patients in the Dexmedetomidine group had an average age of 81.3 (67-92) years. The gender distribution was similar between the two groups with 24 women and 6 men in

the Propofol group, and 17 women and 5 men in the Dexmedetomidine group. Participants in the Propofol group received on average 120.2 (10 – 368) mg of Propofol during surgery, and the Dexmedetomidine group received on average 164 (5.4 – 79.4) µg of Dexmedetomidine.

Variable	All patients (n=52)	Group D (n=22)	Group P (n=30)
Female, n (%)	41 (79)	17 (77)	24 (80)
ASA, n (%)			
I	5 (9.6)	1 (4.5)	4 (13.3)
II	27 (51.9)	12 (54.5)	15 (50)
III	18 (34.6)	9 (40.9)	9 (30)
IV	2 (3.9)	0	2 (6.7)
Age mean (SD)	80.7 (7.6)	81.3 (7.7)	80.3 (7.7)
SPMSQ-score, mean (SD)	9.07 (1.4)	9 (1.4)	9.1 (1.4)
Comorbidities, n (%)			
Hypertension (%)	32 (61.5)	14 (63.6)	18 (60)
Congestive heart failure	8 (15.4)	3 (13.6)	5 (16.6)
Diabetes	7 (13.5)	3 (13.6)	4 (13.3)
Dementia	1 (1.9)	0	1 (4.5)
Stroke	10 (19.2)	6 (27.2)	4 (13.3)
Parkinson's Disease	4 (7.6)	1 (4.5)	3 (10)
COPD	10 (19.2)	3 (13.6)	7 (23.3)
Alcohol Use Disorder	2 (3.9)	1 (4.5)	1 (4.5)
Atrial Fibrillation	14 (26.9)	7 (31.8)	7 (23.3)

Fig. 2. Characteristics of the study population. ASA refers to the American Society of Anesthetists' system of health classification, ranging from I-VI where I is perfectly healthy and VI is dead. COPD is chronic obstructive pulmonary disorder.

Medication/Drug use (%)	All patients (n=52)	Group D (n=22)	Group P (n=30)
Smoking	7 (13.5)	4 (18.2)	3 (10)
Beta blockers	20 (38.5)	11 (50)	9 (30)
Calcium channel blockers	12 (23.1)	6 (27.3)	6 (20)
ACE-Inhibitors/ARB	20 (38.5)	9 (40.9)	11 (36.7)
Statins	15 (28.9)	7 (31.8)	8 (26.7)
ASA	12 (23.1)	7 (31.8)	5 (16.7)
Antidepressants	11 (21.2)	4 (18.2)	7 (23.3)
Bensodiazepines	6 (11.5)	1 (4.5)	5 (16.7)

Fig. 3. Medication/drug use in the study population. ACE = angiotensin converting enzyme. ARB = angiotensin receptor blocker. ASA = acetyl salicylic acid.

Incidence of POD in both groups totaled to 12 patients receiving the diagnosis either clinically ('Delirium outside CAM-ICU') or through CAM-ICU. These means of diagnosis were generally congruent and only differed on a single patient. Out of these 12 patients with POD, 8 were in the Propofol group (incidence: 0.267) and 4 were in the Dexmedetomidine group (incidence: 0.182).

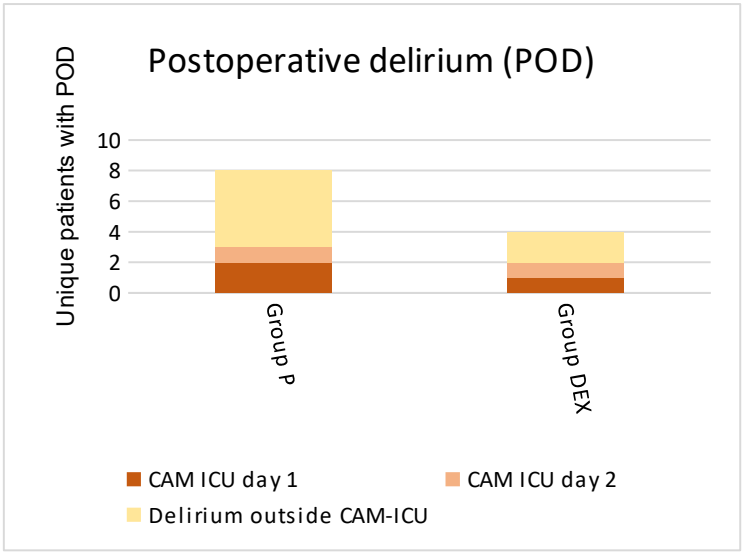

Fig. 3. Events of patients developing POD in the 2 groups during the study period. Each event corresponds to one unique patient developing having failed the Confusion Assesment Method for the Intensive Care Unit (CAM ICU) questionnaire during one of the two days of assessments (CAM ICU day 1/2), or completing the CAM ICU but being determined to suffer from delirium regardless (Delirium outside CAM-ICU). Different colors signify when/how POD was diagnosed. Group P received Propofol, and group D received Dexmedetomidine.

Average LOS in the groups was 9 (4-24) days for the Propofol group and 10 (3-27) for the Dexmedetomidine group. In some patients, the LOS was increased due to non-delirium related adverse events; one patient suffered from hospital-acquired pneumonia, another had a prostate cancer discovered during the inpatient stay, and further one patient suffered a COPD exacerbation requiring oxygen and antibiotic treatment. The former two patients were in the Dexmedetomidine group, while the latter was in the Propofol group.

30 day mortality in the Propofol group was 0.067 (2 deaths) while all patients in the Dexmedetomidine group survived.

The 48-hour opioid dosages for the groups were similar; an average of 56.4mg (15-130) for the Propofol group and 52.5mg (5-110) for the Dexmedetomidine group.

CO2 values were measured through taking 3 intraoperative arterial blood gas (ABG) samples from each of the study participants, see Figure 4.

	ABG #1 PCO2	ABG #2 PCO2	ABG #3 PCO2
Propofol	4.61 (3.9 – 5.3)	5.09 (3.4 – 6.2)	5.06 (4.4 – 5.8)
Dexmedetomidine	4.79 (3.7 – 5.7)	5.02 (4.3 – 5.9)	4.98 (4.2 – 5.8)

Fig. 4. Average arterial blood gas (ABG) carbon dioxide (PCO2) values. Min-max values within parenthesis.

Discussion

In this study we have found that the incidence of POD was lower in the patients given Dexmedetomidine vs those given Propofol. A possibility was that risk factors for developing POD could have varied between the groups and influenced this outcome. Such risk factors include age, sex, cognitive impairment, disability and general comorbidity.[7] Nottingham Hip Fracture Score (NHFS) could also impact the risk of developing POD negatively, but this patient data has not been collected.

For cognitive impairment, we used SPMSQ for inclusion – a score of 7 (1-10 range) or more was required to be included in the study, however, a lower score might imply a mild cognitive impairment that could theoretically predispose one to POD.[11][12] Although, the SPMSQ scores for both groups were similar averaging 9.1 in the Propofol group and 9.0 in the Dexmedetomidine group.

Disability was regarded as visual and hearing impairments as well as Parkinson's disease and previous stroke. We did not document which patients were using hearing aids or glasses, but throughout the study period we had a consensus with both patients and ward personnel that such aids should be worn at all times to minimize the visual or hearing disability's impact on the risk for POD. Still, this remains a weakness of our study.

A past history of stroke was seen in six (Incidence: 0.3) patients in the Dexmedetomidine group and four (Incidence: 0.13) patients in the Propofol group. Two of the stroke survivors in the Dexmedetomidine group developed POD, and two in the Propofol group. Thus, there seems to be an association between previous stroke and development of POD, but despite the Dexmedetomidine group having more stroke survivors, the overall incidence of POD did not increase.

Parkinson's disease was found in one patient in the Dexmedetomidine group (Incidence: 0.045) and three patients in the Propofol group (Incidence: 0.1). Out of those patients, the patient in the Dexmedetomidine group and one patient in the Propofol group developed POD. As with strokes, there is likely a correlation between Parkinson's disease and risk for POD, but unlike with stroke it is less clear if the lower prevalence of Parkinson's patients in the Dexmedetomidine group affected the overall incidence of POD.

The patients in the Dexmedetomidine group were older. Under the assumption that age negatively impacts the risk of developing POD, our study would thus have managed to prevent POD development in this older patient group.

Did the patients in the Propofol group have worse health than the patients receiving Dexmedetomidine, impacting the incidence of delirium?[15] In terms of co-morbid conditions

and general health, the ASA scores in the Dexmedetomidine group were slightly higher (2.4), than in the Propofol group(2.3). Similarily, as age was higher in the Dexmedetomidine group, one would expect this to enhance the incidence of POD, but this was not so.

Further, depression is an independent risk factor for developing delirium.[16] We did not screen for depression, but as noted in the medication lists of patients in both groups, antidepressants were more common in the Propofol group (n=7) than in the Dexmedetomidine group (n=4). However, only one patient in the Propofol group and two patients in the Dexmedetomidine group taking antidepressants developed POD. Thus, the prevalence of antidepressant use cannot explain the difference in POD incidence. However, lack of antidepressant medication *per* se does not exclude depression – some patients might have depression without receiving medication.

Similarly, benzodiazepine use is associated with an elevated risk for developing delirium.[17] In the Propofol group 3/5 patients and 1/1 patient in the Dexmedetomidine group having prescriptions of benzodiazepines developed POD. Thus, benzodiazepine use may be a confounding factor and will be important to explore in future studies.

Gender spread was similar between groups; Dexmedetomidine group had 5 men and 17 women, while the Propofol group had 6 men and 24 women.

LOS was longer for the patients receiving Dexmedetomidine and could depend on a higer age and ASA class in these patients vs. those given Propofol.

The sedation affected CO2 values marginally in both groups.

We excluded 17 patients from the study. Out of them, the largest group of patients were excluded because they were being planned for general anesthesia (7 patients). Following that, 4 patients were excluded because of a dementia diagnosis or having an SPMSQ of less than 7. 2 patients declined to complete the post-operative CAM-ICU assessments. One patient had delirium on arrival to the hospital, and another was transferred to a different hospital. Another patient was misdiagnosed as having a hip fracture, and the last patient to be excluded had simultaneously been enrolled into a conflicting study.

The exclusions may have had an impact on our results especially in the cases of the patients who had SPMSQ <7. It should be clear that it is not ethical to recruit patients with dementia into studies, as they cannot give informed consent. However, with the patients that did not have a dementia diagnosis but a low SPMSQ score, there could have been a merit to recruiting them, as long as excluding the risk of them having a dementia diagnosis not found in the hospital documentation was possible, which it wasn't. Because of this, had we recruited the patients with SPMSQ <7, it is possible that we would have had more cases of POD owing to dementia.

Regarding the patients that declined to finish the study, they both did so after surgery. In both cases, the patients were cognitively clear and spoke at length with the examiner about how they were feeling and their reasoning for not wishing to complete the study. In both cases, their reason was that they were feeling very tired after the surgery.

Regarding the patients that were excluded due to being planned for general anesthesia, this planning was generally due to the anesthetist in charge wishing to do so, and not because of the patients necessarily being sicker. Had these patients received sedation and not general anesthesia, they would likely have performed similarly to the patients we did include.

Limitations

When it comes to limitations of our study, the sample size of this study was too small. This is an interim report of about half of patients planned to be included. This may explain that the difference in incidence of POD between the groups is **not** statistically significant. We used Fisher's exact test, using significance levels of .05 and .10, and further verified with a binomial proportion test using the same significance levels. In both, the outcome was outside of the ranges for statistical significance. With this said, the difference in POD incidence was fairly large despite that the prevalence of risk factors for POD were slightly higher in the Dexmedetomidine group. If the incidence of POD in both groups (18.2% and 26.7% respectively) continues to follow the results of this study, we would be estimated to require approximately 750 participants, and 375 in both groups, to achieve a power of 0.80 and a P-value <0.05.

SPMSQ questionnaire items are related to news and politics, such as the names of the current and previous Prime Minister of Sweden. Therefore, it is very possible that a mentally alert person but not up date with this would miss out on some points. Likewise, questions including basic mathematics could be passed by a highly educated person despite suffering from a fairly severe cognitive impairment. With this in in mind – the SPMSQ to assess cognitive status has weak points.

Further limitations includes the accuracy of diagnosing delirium as patients may be delirious and still have a negative CAM-ICU. However, systematic reviews of different screening methods for delirium have shown that it is among the most sensitive, specific and simple to administer screening methods.[18][19] We did see all of the patients over a period of 48-72 hours and although we had support from ward nurses and doctors in assessing their mental

status and eventual deviation from baseline, it is possible that some cases of POD could have been missed. Nevertheless, it is likely to assume that a positive CAM-ICU and/or a clear clinical diagnosis of delirium would imply a more severe case of POD with greater risk for adverse patient outcomes.

Another possible lesson to be learned from this study is that the timing and frequency of CAM-ICU assessments might impact the diagnosis of delirium. We aimed to see the patients shortly after 24 hours had passed following surgery, and then on the same time on day two. However, this also means that in some cases, we might have met the patients shortly after they were administered medications such as opioids, which affect wakefulness. It is therefore possible that some patients could have had a positive CAM-ICU due to medication side effects affecting their performance, but not truly have been delirious. A suggestion for future studies to circumvent this problem would be to conduct CAM-ICU twice a day; once in the morning and once in the afternoon.

Furthermore, there might have been problems with bias. The individuals conducting the CAM-ICU assessments were not blinded, and fully aware of whether the study participant had received Propofol or Dexmedetomidine. We cannot be certain that this knowledge did not affect our perception of the patients and their mental status. This becomes further complicated when considering the patients who were diagnosed with delirium outside of CAM-ICU, as, even though such diagnoses were corroborated with ward nurses and other personnel, it is still a very subjective means of diagnosis. With this in mind, a future study should ensure that the individuals conducting CAM-ICU assessments are unaware of what medication the study patient has received.

Lastly, there is the issue of bi-spectral analysis (BIS). While all the study participants were monitored with BIS during surgery to assure an adequate level of sedation, we failed to take heed of its possible relevance for risk of developing delirium following surgery. Because of this, we don't have data on the individual BIS scores for each patient and cannot draw any conclusions on whether depth of sedation during surgery impacted the outcomes of the patients. This will be important to explore in future studies.

With this said, we believe there are hints that surgical sedation with Dexmedetomidine may lower the incidence of POD in geriatric patients with AHF. When this interim study, here presented, is further completed (n=120) it might show greater differences between the two groups, pointing towards this notion.

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17. https://www.ncbi.nlm.nih.gov/pubmed/21372278 *"Brief report: preoperative frailty in older surgical patients is associated with early postoperative delirium.", Leung, Tsai, Sands, 2011*

18. https://www.ncbi.nlm.nih.gov/pubmed/19326492 *"Executive function and depression as independent risk factors for postoperative delirium.", Smith et al, 2009*

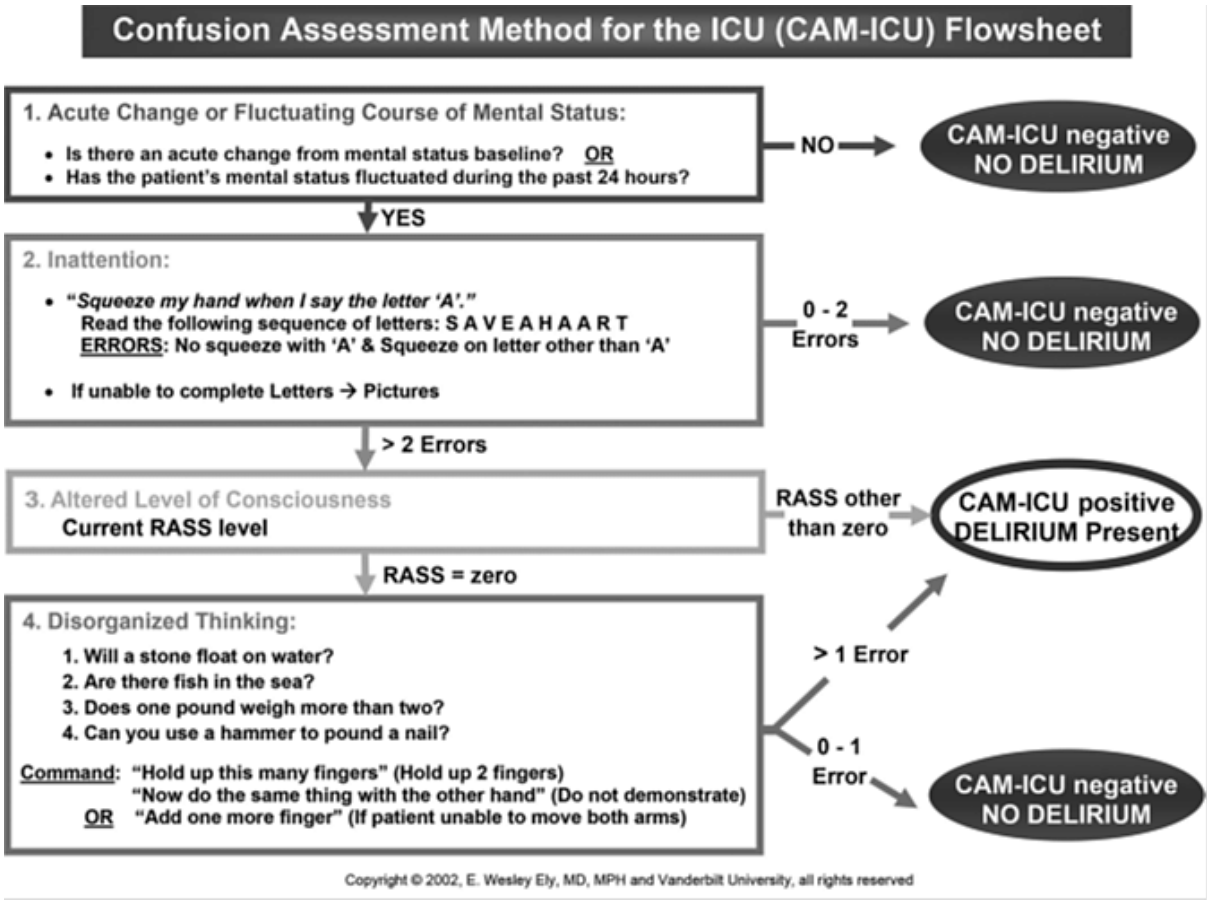
19. https://www.ncbi.nlm.nih.gov/pubmed/29284416 *"Preoperative medication use and postoperative delirium: a systematic review.", Kassie et al, 2017*

20. https://www.ncbi.nlm.nih.gov/books/NBK82554/ *"Delirium: Screening, Prevention, and Diagnosis – A Systematic Review of the Evidence", Greer et al, 2011*

21. https://www.ncbi.nlm.nih.gov/pubmed/18384586 *"The Confusion Assessment Method: a systematic review of current usage." Wei, Fearing, Sternberg & Inouye, 2008*

Appendix

1. CAM-ICU Flowsheet



Patients were assessed for prevalence of delirium on days 1 and 2 following surgery using the above flowsheet.

As Richmond Agitation-Sedation Scale (RASS) is not used in geriatric or orthopedic care, step 3 was omitted in the assessments.

Nytt sövningsmedel kan minska risken för förvirring efter operation för bruten höft

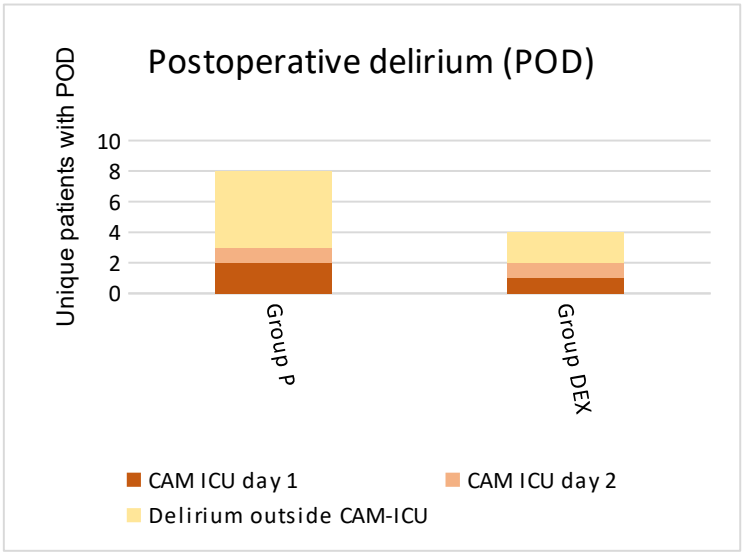
Förvirringstillstånd sker relativt ofta efter operationer hos äldre är ett stort problem för vården av särskilt patienter som har brutit höften. Förutom att förvirring är väldigt traumatiskt för såväl patienter som deras anhöriga, ökar även tiden på sjukhus, risken för komplikationer och risken för död inom 30 dagar.

Dexmedetomidin (Dexdor®) är ett läkemedel som man inom intensivvården använt för att söva och behandla patienter med förvirringstillstånd, med goda resultat. Nyligen har Dexdor® blivit godkänt för att användas för sövning för operation, och visst tidigare data tyder på att det kan minska risken för att utveckla förvirring. På grund av detta var vårt syfte med denna studie att undersöka Dexdor® effekt på risken för förvirring.

Utöver detta valde vi också, utifrån tidigare forskningsresultat och tankar om Dexdor® effekter, att se närmre på om längd av tid på sjukhus, överlevnad efter 30 dagar, behov av smärtstillande mediciner efter operation och koldioxidvärden under operation påverkas av Dexdor®. Vi valde att jämföra resultaten med Propofol®, som är ett väl använt medel för sövning under operationer.

Vi rekryterade patienter som kom in akut med bruten höft på Mölndals sjukhus under en period från september 2019 till april 2020, och delade slumpmässigt in dem till att få antingen Propofol® eller Dexdor®. Efter detta följde vi patienterna under två dygns tid där vi träffade dem en gång per dag för samtal och undersökning för att diagnosticera förvirringstillstånd. Vårdtidens längd, doser av smärtstillande läkemedel och koldioxidvärden under operation hämtades ut från sjukhusjournaler.

Vi nådde fram i en slutgiltig total på 52 patienter. Av dessa fick 30 st Propofol® och 22 st Dexdor®. Vi såg att färre patienter drabbades av förvirring efter operation i gruppen som fick Dexdor®, 18.2%, än i gruppen som fick Propofol®, 26,7%. Tid på sjukhus, bruk av smärtstillande mediciner och koldioxidvärden skiljde sig inte nämnvärt mellan grupperna.



Vår studie tyder hittills på en lägre risk för att drabbas av förvirring efter operation om patienterna sövdes med Dexdor®, men vi kan i dagsläget inte säkert säga om detta resultat är helt oberoende av slumpen. Denna text är en deltidsrapport av en studie som kommer pågå under längre tid och ha med långt fler patienter än vi redovisar idag.

För att kunna konstatera att detta samband faktiskt finns, hoppas vi att studien, när den är klar och har nått upp i 60 patienter per grupp, kommer kunna avfärda risken för att skillnaden bygger på slump. Med detta sagt är Dexdor® ett lovande läkemedel för kirurgisk sövning och ett klart ämne för fortsatt forskning.