Delirium in older people after cardiac surgery

-risk factors, dementia, patients' experiences and assessments

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En dag ska vi dö, alla andra dagar ska vi leva.

Per Olov Enquist

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Abstract

Background:

Delirium is common in older people undergoing cardiac surgery. Delirium is an acute or subacute neuro-psychiatric syndrome, characterized by a change in cognition, disturbances in consciousness; it fluctuates, develops over a short period of time and always has an underlying cause. It is associated with a disturbance in psychomotor activity, and is classified according to different clinical profiles such as hypoactive, hyperactive and mixed delirium. Delirium after cardiac surgery is not harmless, it increases the risk of complications such as prolonged stay in hospital, falls, reduced quality of life, reduced cognitive function and increased mortality.

Aim:

The overall aim of this thesis was to investigate postoperative delirium in older people undergoing cardiac surgery with Cardiopulmonary Bypass (CPB), focusing on risk factors, dementia and patients' experiences; and to evaluate an assessment for screening delirium.

Methods:

This thesis compromises four studies. All participants (n=142) were scheduled for cardiac surgery with use of CPB at the Cardiothoracic Surgery Department, Heart Centre, Umeå University Hospital, Sweden, between February and October 2009. Six structured interviews were conducted preoperatively, day one and day four postoperatively, and in home visits, one, three and five years after surgery (2010, 2012 and 2014). The assessment scales used in Studies I, II and IV were: the Mini-Mental State Examination (MMSE) for cognition, the Organic Brain Syndrome Scale (OBS) for delirium, Geriatric Depression Scale 15 (GDS-15) for depression, Katz staircase with Activities of Daily Living (ADL) for participants' functional status and the Numerical Rating Scale (NRS) for pain. During the hospital stay, nursing staff used the Swedish version of the Nursing Delirium Screening Scale (Nu-DESC) to assess delirium. Semi-structured interviews were also carried out (III) in the one-year follow up. Delirium, dementia and depression were diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders (DSM IV TR).

Results:

Out of 142 participants 54.9% (78/142) developed delirium after cardiac surgery (I). Independent risk factors, predisposing and precipitating, associated with delirium were: age, diabetes, gastritis/peptic ulcer, volume load during operation, longer time on ventilator in intensive care, increased temperature and plasma sodium concentration in the intensive care unit. Out of 114 participants thirty (26.3%) developed dementia within the five years of follow-up. It was shown that a lower preoperative MMSE score and postoperative delirium were factors independently associated with development of dementia (II). One year after cardiac surgery, participants diagnosed with postoperative delirium described in detail feelings of extreme vulnerability and frailty. Despite this, the participants were grateful for the care they had received (III). Hypoactive was the most common symptom profile for delirium. The Swedish version of Nu-DESC showed high sensitivity in detecting hyperactive delirium, but low sensitivity in detecting hypoactive delirium (IV).

Conclusion:

Delirium was common among older patients undergoing cardiac surgery. Both predisposing and precipitating factors contributed to postoperative delirium. Preventive strategies should be considered in future randomized studies. It might also be suggested that cognitive function should be screened for preoperatively and patients who develop delirium should be followed up to enable early detection of symptoms of dementia. Whether prevention of postoperative delirium can reduce the risk of future dementia remains to be studied. To minimise unnecessary suffering, patients and next of kin should be informed about and prepared for the risk of delirium developing during hospitalization. The Swedish version of Nu-DESC should be combined with cognitive testing to improve detection of hypoactive delirium, but further research is needed. Healthcare professionals need knowledge concerning postoperative delirium in order to prevent, detect and treat delirium so as to avoid and relieve the suffering it might cause.

Keywords:

Cardiac surgery, Cardiovascular disease, Delirium, Dementia, Nursing, Older people, Patients' experiences, Perioperative period

Abbreviations

CABG	Coronary artery bypasses grafting
CAM	Confusion Assessment Method
CAM-ICU	Confusion Assessment Method for Intensive Care
CSD	Cardiothoracic Surgery Department
CVD	Cardiovascular diseases
CPB	Cardiopulmonary Bypass
DSM-IV-TR	Diagnostic and Statistical Manual of Mental Disorders fourth Edition- Text Revision
EN	Enrolled nurse
GDS-15	Geriatric Depression Scale, 15 item version
ICDSC	Intensive Care Delirium Screening Checklist
ICU	Intensive care unit
I-ADL	Instrumental-activities of daily living
Katz ADL	The Katz Staircase and the Katz ADL index
MCI	Mild cognitive impairment
MMSE	Mini-Mental State Examination
NRS pain	Numerical Rating Scale of pain
NU-DESC	Nursing Delirium Screening Scale
OBS	Organic Brain Syndrome Scale
P-ADL	Personal-activities of daily living
POCD	Postoperative Cognitive Dysfunction
POD	Postoperative delirium
PODCS	Postoperative delirium after cardiac surgery
RN	Registered nurse
SSD	Subsyndromal delirium

Sammanfattning på svenska

(Summary in Swedish)

Akut förvirringstillstånd (delirium) hos äldre personer som genomgått hjärtkirurgi –riskfaktorer, demens, patienternas erfarenheter och skattningsinstrument.

Bakgrund:

Delirium är vanligt hos äldre personer som genomgår hjärtkirurgi. Delirium är ett akut eller subakut neuropsykiatriskt syndrom, som kännetecknas av förändrad kognitiv förmåga samt en förändad medvetande nivå. Delirium utvecklas under en kort tidsperiod, tenderar att fluktuera och har alltid en bakomliggande orsak. Delirium kan klassificeras som hypoaktivt, hyperaktivt eller en blandform av båda dessa. Delirium efter hjärtkirurgi kan öka risken för andra komplikationer som tillexempel; förlängd vårdtid, fall, försämrad livskvalité, nedsatt kognitiv förmåga samt mortalitet.

Syfte:

Det övergripande syftet med denna avhandling var att undersöka postoperativt delirium bland äldre personer som genomgått hjärtkirurgi med hjärt-lungmaskin med fokus på riskfaktorer, demens, patienters erfarenheter samt utvärdering av skattningsinstrument för delirium

Metod:

Denna avhandling består av fyra studier. Alla deltagare (n = 142) genomgick rutinmässig hjärtkirurgi med hjärt-lungmaskin vid Thoraxkirurgiska kliniken, Hjärtcentrum, Umeå Universitetssjukhus, mellan februari till oktober 2009. Sex intervjuer genomfördes; preoperativt, dag ett och dag fyra postoperativt, samt vid hembesök ett, tre och fem år efter operationen (2010, 2012 och 2015). Skattningsinstrument som användes i studie I, II och IV var;

The Mini-Mental Test (MMSE) för kognition, The Organic Brain Syndrome Scale (OBS) för delirium, Geriatric Depression Scale (GDS-15) för depression, Katz ADL trappa-Katz-index aktiviteter för dagliga livet och Numerisk Rating Scale (NRS) för smärta. Under vårdtiden använde vårdpersonalen Nursing Delirium Screening Scale (Nu-DESC) tre gånger dagligen för att skatta delirium. Nu-DESC jämfördes med en sammanvägning av MMSE och OBS-skalan. Vid uppföljningen år 2010 genomfördes dessutom semistrukturerade intervjuer. Delirium, demens och depression diagnostiserades enligt Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR).

Resultat:

Studie I visade att 54.9% (78/142) av patienterna utvecklade delirium efter hjärtkirurgi. Oberoende riskfaktorer (bakomliggande och utlösande) för

delirium var; ålder, diabetes, gastrit/magsår, volymbelastning under operation samt respiratortid, förhöjd kroppstemperatur och förhöjd natriumkoncentration i plasma på intensivvårds avdelning. Studie II visade att 26.3% (30/114) av deltagarna utvecklade demens under en femårs uppföljning. En nedsatt preoperativ kognitiv förmåga (indikerad av lägre MMSE-poäng) och förekomsten av postoperativ delirium var faktorer som ökade risken för att utveckla demens. Ett år efter operation kunde deltagarna som diagnostiserats med postoperativt delirium i detalj beskriva sin sårbarhet och skörhet under vårdtiden. Deltagarna beskrev också sin tacksamhet över den vård de fått (Studie III). Den vanligaste formen var hypoaktivt delirium. Den svenska versionen av Nu-DESC kunde upptäcka hyperaktivt men inte hypoaktivt delirium (Studie IV).

Slutsats:
Delirium var vanligt bland äldre patienter som genomgått hjärtkirurgi. Både bakomliggande och utlösande faktorer utgjorde ökad risk för att utveckla postoperativt delirium. Förebyggande strategier bör övervägas i framtida randomiserade studier. Kognitiv funktion bör skattas preoperativt och patienter bör skattas för delirium under vårdtiden och följas upp efter hemgång för att upptäcka tidiga demenssymtom. Huruvida förebyggandet av postoperativt delirium kan minska risken för demens senare återstår att studeras. För att minska onödigt lidande bör patienter och anhöriga bli informerade och förberedda på risken att utveckla delirium under vårdtiden. Den svenska versionen av Nu-DESC behöver förmodligen kombineras med ett kognitiv test för att upptäcka hypoaktivt delirium. För att lindra det lidande som syndromet kan orsaka behöver vårdpersonal fördjupad kunskap i syfte att förebygga, upptäcka och behandla postoperativt delirium.

Original papers

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II. Claesson Lingehall, H., Smulter, N., Lindahl, E., Lindkvist, M., Engström, KG., Gustafson, Y., Olofsson, B. Dementia after postoperative delirium in older people who have undergone cardiac surgery: a longitudinal cohort study. In manuscript (2016).

III. Claesson Lingehall, H., Smulter, N., Olofsson, B., Lindahl, E. Experiences of undergoing cardiac surgery among older people diagnosed with postoperative delirium: one year follow-up. BMC Nurs. 2015; 14: 17.

IV. Lingehall, HC., Smulter, N., Engström, KG., Gustafson, Y., Olofsson, B. (2013). Validation of the Swedish version of the Nursing Delirium Screening Scale used in patients 70 years and older undergoing cardiac surgery. J Clin Nurs. 2013; 22 (19-20):2858-66.

Introduction

A growing number of older people are undergoing cardiac surgery as a result of advances in pharmacological treatments, developments in surgery and anaesthetic techniques. Cardiac surgery is now considered a safe procedure. However, mental disorders and neurological complications, such as acute confusion (delirium), are reported in postoperative care (1, 2). Postoperative delirium after cardiac surgery is not harmless. It increases the risk of further complications including reduced quality of life and reduced cognitive function in the first year after surgery (2, 3).

During my work as an anaesthetist nurse I developed an interest in postoperative delirium as I became aware that many patients were delirious after cardiac surgery and seemed to be suffering because of it. Those patients were often seen as 'difficult patients' and when agitated and anxious, they increased the burden on the staff. My experience was also that there was an attitude of general acceptance towards delirious patients, that 'delirium is common and there is nothing much to be done about it' or that it 'is a benign syndrome elderly people often suffer and usually disappears before discharge'. In the literature, in 2008, knowledge about the detection, prevention and treatment of delirium in older people after cardiac surgery was limited. On becoming a PhD student my intention was to increase the knowledge about delirium after cardiac surgery.

Background

Delirium after cardiac surgery should, in this thesis, be understood as part of a context of cardiac surgical treatment, aging and dementia.

Delirium

This section presents delirium, first in a general context and then focusing on delirium after cardiac surgery.

Hippocrates first described the symptoms of delirium as early as 2,500 years ago but Celsus was the first to use the term “delirium”, in the first century A.D. “Phrenitis”, “confusion” (4) and “intensive care syndrome” (5) are other expressions that have been used to describe delirium. When cardiac surgery was established and cardiopulmonary bypass (CPB) became a routine procedure, delirium was described as a serious problem. Expressions such as “madness in the recovery room“ (6) or “postcardiotomy delirium” (7) were used. The Diagnostic and Statistical Manual of mental disorders (DSM) is often used today in setting a delirium diagnosis. The diagnosis and names of the syndrome have varied: DSM-I (1952) and DSM-II (1968) used “acute organic brain syndrome (ACS)” (8). “Delirium” was used in DSM-III (1980), DSM-III-R (1987), DSM-IV (1994), DSM-IV-TR (9) and DSM-5 (10). Increased knowledge about delirium has contributed to new diagnostic criteria in DSM. In this thesis postoperative delirium after cardiac surgery (PODCS) is evaluated in accordance with the DSM-IV-TR (9).

Delirium is not considered a disease; it is an acute neuro-psychiatric syndrome. Delirium can occur in all ages but is more common in older people. The syndrome is characterized by a change in cognition, disturbances in consciousness, seems to fluctuate, develops over a short period of time and always has an underlying cause (Table 1) (9). The symptom profile of delirium can change over time in individuals, and can present as four types of psychomotoric activities: hypoactive, hyperactive, a mixture of hyper- and hypo-active and non-classifiable symptoms (11, 12). Hypoactive delirium is not easy to recognize since the patient is usually calm and quiet and can be seen as inactive, inattentive or apathetic. Hyperactive delirium is characterized by mental and physical restlessness, irritability and anger and is easily recognized (11, 13). Patients with non-classifiable symptoms cannot be diagnosed according to the first three psychomotor activities. Delirium includes a wide variety of psychiatric symptoms such as anxiety and depression (11, 14). One study shows that in patients undergoing cardiac surgery the majority (83%) had an emotional PODCS with anxiety and depressed mood (15). There is also evidence for differences in the psychiatric symptoms of delirium in patients with and without dementia. Lundström et al (2012) demonstrated that in patients with hip fracture, emotional delirium was more common in those with dementia, while psychotic symptoms were more common in those without dementia (16). Delirium may not be recognized in a patient with cognitive decline when the decline is due to dementia (17). Improved knowledge of psychiatric and psychotic symptoms may increase the awareness of delirium among staff. There is a need for individual treatment and care that can reduce the risk of further disturbances in brain functions (11).

Subsyndromal delirium (SSD) does not meet the DSM criteria for delirium. SSD represents an intermediate state that differs from both clinical delirium and a normal neurologic state without delirium. SSD has been investigated after cardiac surgery (18), among older people in other populations (19) and in ICUs (20, 21). Even if SSD is described as only a mild cognitive disorder it seems to have clinical relevance as it increases the mortality risk (20).

Table 1. Presents the–Diagnostic and Statistical Manual of Mental Disorders, 4th edition-Text Revision, criteria for delirium.

A. Disturbance of consciousness (i.e. reduced clarity of awareness of the environment) with reduced ability to focus, sustain or shift attention.
B. A change in cognition or the development of a perceptual disturbance that is not better accounted for by a pre-existing, established or evolving dementia.
C. The disturbance develops over a short period of time (usually hours to days) and tends to fluctuate during the course of the day
D. There is evidence from the history, physical examination or laboratory findings that the disturbance is caused by the direct physiological consequences of a general medical condition.

Already, 1965 when CPB was introduced as routine, neurological, psychiatric and intellectual complications after cardiac surgery were found and investigated (22). In cardiac surgery, neurological complications were first classified into Type 1 and Type 2 injuries (23). Type 1 includes a new, transient ischemic attack, stroke or brain death. Type 2 is more common and includes postoperative cognitive dysfunction (POCD) and PODCS (23-25). In Type 2, POCD is a mild form of perioperative ischemic brain injury, which emerges as deterioration in memory, reduced attention and decreased concentration after cardiac surgery (26) and also affects the quality of life (24). A review investigating POCD after cardiac surgery showed that 50-70% of patients experienced cognitive decline soon after surgery. After 2 months this number was reduced to 30-50% and then to 10-20% at one-year follow-up (25). The circumstances in which POCD can be a risk factor for dementia remain uncertain (27). However, studies investigating POCD are difficult to interpret when different definitions of cognitive impairment, different neuropsychological tests and different timing of postoperative measurement are used (25). As Patel et al 2015 stated “it is possible that patients may be exceeding a "threshold" of pre-existing vulnerability where the brain's ability to compensate for injuries or inflammation during surgery is absent” (25).

The prevalence and incidence of delirium differ between populations. The prevalence of delirium among very old people living at home and in institutions is 17-39% (28), among emergency admissions to hospital it is 9-23%(29), among medical in-patients 10-31% (30), and in palliative care 13-42% (31, 32). The incidence of delirium in paediatric care is 10-25% (33, 34), in ICUs 48-75% (35, 36), among patients with hip fracture 62-75% (37, 38), in the recovery room 14-45% (39, 40) and after cardiac surgery with CPB 23-48% (41, 42). As shown, delirium is common and the highest incidence seems to be among patients with hip fracture, in the ICU and after cardiac surgery.

The pathophysiology of delirium seems not to be fully understood. However, there are a number of theories or hypotheses that have been proposed to explain the processes leading to delirium. A few examples are the oxygen deprivation hypothesis, the neuronal aging hypothesis, and the inflammatory hypothesis (43).

Several risk factors for delirium are described in the literature but no single cause has been identified and the underlying causes seem to be multifactorial (43-45). Delirium is sometimes the first and only symptom of an underlying disease (predisposing factor) or a side effect of the medical management (precipitating factor). One possible explanation is that predisposing factors affect the brain function and can lead to a reduction or imbalance in neurotransmitters in the brain (46). The aging process can cause reduced brain-reserve capacity, which makes older patients more vulnerable and thus more prone to delirium (29, 45, 47). Therefore delirium may indicate an unrecognized, reduced brain-reserve capacity.

Below, I have chosen to focus on risk factors for delirium after cardiac surgery. Several of the predisposing risk factors affect the capacity to process perceptions such as increasing age (15, 48, 49), reduced cognitive function (42, 48, 50) and aspects of mental health such as depression (48) while others directly or indirectly affect vascular health in terms of, for example, stroke, cardiovascular diseases (CVD) and diabetes (48, 51). There is a wide range of precipitating factors described in the literature, and they appear to be the results of different treatments during cardiac surgery. When cardiac surgery began the precipitating factors were recognized and named as “a new disease of medical progress” (5). The precipitating mechanism of delirium in patients undergoing cardiac surgery differs from other populations. These patients are vulnerable and have a high prevalence of cardiovascular and cerebrovascular disease. In addition, the use of CPB results in a systemic inflammatory response (52), changes in cerebral blood flow and cerebral oxygenation (53). I have chosen to group precipitating factors for PODCS into two groups. The first group comprises risk factors that seem to cause oxygen and neurotransmitter imbalance. These are hypoxia, anaemia, red blood cell transfusion, prolonged ventilator time, CPB surgery, duration of surgery, increase of inflammatory markers such as cytokines and interleukin-6, plasma cortisol level, use of inotropic medications and the use of sedation (48, 49, 51, 54). The second group comprises somatic conditions and complications after surgery that might directly or indirectly affect brain function, and thereby cause delirium. These are infections, cardiogenic shock, pneumonia and arterial fibrillation (48, 51). The risk of developing delirium increases proportionally with the number of predisposing and precipitating risk factors (55).

There is a lack of knowledge about the underlying causes of PODCS among older people. Knowing about potential risk factors for PODCS may help healthcare professionals, through their risk evaluation prior to surgery, to improve clinical care and hopefully reduce unnecessary suffering.

Assessments of delirium

Despite the common prevalence and incidence of delirium, the syndrome is often underdiagnosed. Eriksson et al (2002) investigated recognition of delirium in postoperative care after cardiac surgery. This study included 52 patients and 12 of them developed PODCS. None of these patients were documented as delirious in the medical records, either by nurses or physicians (15). This can probably be attributed to a general acceptance or lack of knowledge about delirium, and leads to lack of recognition of delirium symptoms (15, 56). A similar picture was presented in a study among patients with hip fracture which reported that nurses diagnosed delirium almost twice as often as physicians. One possible explanation for this may be that nurses spend more time with the patients (57). Nevertheless, healthcare professionals seem to fail to diagnose delirium in almost three out of four patients (58, 59). An assessment for delirium used routinely and systematically may lead to improved staff awareness about delirium and is important for patient health (60, 61). When an assessment for delirium was used in the ICU the use of antipsychotic medications increased (62).

A large number of assessment scales for the detection of delirium have been developed over the last 20 years for various populations, but there is no consensus about which scale is to be preferred or which is best (63-65). Many delirium scales are developed for research purposes and seem to be too time consuming or require too much staff training and patient participation to be easily applied in clinical practice (63, 66). However, delirium might also be difficult to detect because of the lack of understanding regarding the syndrome. Nurses and physicians need training and education in recognizing delirium (67-70). The most commonly used delirium assessment is the Confusion Assessment Method (CAM) (71). When it was developed at the beginning of the 1990s, it was said to be reliable and valid for identifying delirium being based on observations. But later studies have shown that it is difficult for nurses to use CAM in clinical care, especially without a complementary cognitive assessment (56, 72, 73). In ICUs, in patients with limited ability to answer questions, two commonly used assessments are the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) (74) and the Intensive Care Delirium Screening Checklist (ICDSC) (75). The CAM-ICU (76) and ICDSC (77) have been translated into Swedish and validated for use in ICUs in Sweden.

To my knowledge (2008), there is no assessment for delirium that is available for nurses to use in their daily routine care in Sweden, and is validated for cardiac surgery patients. The Nursing Delirium Screening Scale (Nu-DESC), developed in 2005, is based on nurses' observations during a whole shift and is considered to be fast (1-2 minutes). It has been shown that Nu-DESC has high sensitivity for detecting delirium (78, 79) and seems to be a user-friendly assessment for detecting delirium in oncology care (78), the recovery room (39), surgical ward (80), and intensive care unit (64) However, Nu-DESC has neither been translated into Swedish nor validated for older people undergoing cardiac surgery.

Consequences of delirium

In older people delirium appears not only to be a marker of a vulnerable patient, it is also associated with poor outcome (45). Delirium may lead to patients hurting themselves, for example they extubate themselves, remove their catheters and sustain bruising (81). Patients who developed PODCS have a greater prevalence of falls (82), a longer hospital stay (83, 84), more frequently need home health services, are more often discharged to a nursing home (82), a reduced quality of life and an increased risk of dying (85, 86). Studies show that PODCS may lead to cognitive dysfunctions in a time-frame of six months to one year after cardiac surgery (2, 3). However, there is a lack of longitudinal studies investigating the impact on PODCS among older patients undergoing cardiac surgery.

Patients' experiences

Studies show that patients' mental health is affected after cardiac surgery which leads to psychological suffering. As early as 1965, delirium was described as a "psychiatric complication of open heart surgery" (22). Even then, patients were asked about their experiences of their time in hospital. They described the atmosphere during postoperative care as frightening. Illusions were described caused by new, unusual sounds from air-conditioners, or reflections from oxygen tents that could change into something else. Patients did not report their experiences to the staff, at least not until more dramatic things happened (22). In the mid-1970s, in Sweden, Aberg (1974) investigated the effect of open heart surgery on intellectual function. During the one-year follow-up one participant spontaneously spoke about the terrifying experience of not being able to communicate or to move and believing that the care giver was a prison guard (87). Twenty years later, from 1990 to 2015, a number of articles were published aimed at illuminating patients' experiences of delirium. These articles investigated patients' experiences of delirium mainly during or soon after a hospital stay in orthopaedic (88-90), intensive (91-93), oncology (94), geriatric (95, 96) and geriatric or medical-surgical care (95, 97). Laitinen (1996) carried out an interview study among patients undergoing cardiac surgery early after the surgery and during their hospital stay. Patients described their experiences of delirium in the ICU as an incomprehensible experience with feelings of anxiety and being somewhere in between consciousness and unconsciousness (98). Another study, also among patients undergoing cardiac surgery, the hospital stay was described as a mostly positive experience, despite discomfort, illness, isolation, feelings of hopelessness and memory losses (99).

Understanding patients' experiences of reality while experiencing delirium can provide nursing staff with tools with which to better comprehend and help patients and thus provide security during the delirium episode (90). However, delirium is a frightening experience and may lead to suffering among older people (95). Healthcare professionals know about treatment for CVD and cardiac surgery procedures but they are not always aware of patients' experiences of illness, or care or of PODCS. To my knowledge few studies have focused on older patients' experiences of undergoing cardiac surgery or delirium after cardiac surgery or their long-term memories and how this might affect them one year after surgery.

Delirium prevention and treatment

Today there is no convincing evidence that pharmacological interventions can prevent delirium (45). However, the choice of anaesthetic medications can reduce the incidence of PODCS (100, 101). Studies show that delirium may be prevented and treated by means of non-pharmacological interventions in hospitalized older patients in different populations (37, 102-105). These interventions should be multifactorial and combined with both nursing and geriatric interventions, to succeed in reducing the risk of delirium. The intervention should include among others mental stimulation, early mobilization, ensuring optimal audiovisual or hearing conditions, non-pharmacological approaches to promote sleep, maintaining nutrition and hydration, preventing hypoxia, pain relief, and treatment of constipation and urinary tract infections (37, 103, 104). Studies have also shown that design and organization of hospital rooms can reduce the incidence of delirium (106-108). Nurses need to be aware that older patients are so vulnerable that even minimal sleep deprivation or a small dose of a sedative might be enough to precipitate delirium (45).

It has been suggested that the occurrence of delirium is a marker for quality of care (109, 110). Nurses are close to patients, responsible for the care provided and ideally situated to detect, prevent and treat delirium as they spend a large amount of time at the bedside (56, 111).

Cardiac surgery

Cardiac surgery is a lifesaving procedure for older people with CVD, and for some patients the only chance of relieving symptoms and reducing the risk of death (112). Despite declining trends in mortality, CVD remains the leading causes of death worldwide. In Sweden CVDs are the most common cause of death (37%) followed by cancer (26%) (113). CVDs include numerous heart and vessel problems many of which are related to atherosclerosis (114, 115). Reported risk factors for CVDs are unhealthy diet, physical inactivity, diabetes, hypertension and high blood lipids (115). The treatment recommendations for CVD are lifestyle changes and pharmacological treatments, as well as catheter-based and surgical interventions (116, 117).

Modern cardiac surgery was developed when CPB was established in the early 1950s. It was designed to replace the functions of both lungs and heart enabling surgeons to repair the heart while the patient's cardiac circulation was suspended. The first cardiac surgery with CPB was carried out in 1953 in the USA (118) and shortly afterwards the second was conducted in Sweden (119, 120). The first coronary bypass surgery (CABG) was carried out more than ten years later, in 1967 (121). So when cardiac surgery was established as a routine treatment for CVD, it gave millions of people a "new chance" at life. At the start only younger people were accepted for surgery but today, technological advances, developments in surgery and anaesthetic techniques have made it possible to offer even older people cardiac surgery. In Sweden more than 5600 cardiac surgeries were performed in 2014. The most common procedure is isolated CABG but cardiac surgery often includes more than one type of procedure, such as CABG and valve, and valve and aortic surgery (117). In 2014 approximately 40% of the patients undergoing cardiac surgery were aged 70 years and above, and almost 10% were 80 years and above. Recently, pharmacological treatments, developments in medical devices and care have resulted in a fall in the number of cardiac surgeries, by approximately 3% each year. Thus, fewer but older people are undergoing cardiac surgery today and the mortality rate is still decreasing. Improved health care is also reflected in a decline in mortality after cardiac surgery despite the patients being steadily older (117).

Aging

The prevalence of old people (>60) is increasing globally and they now comprise over 12% of the world population. The number is expected to rise in the years to come. Europe has one of the oldest population in the world with around 24% over the age of 60, and the number estimated to increase to approximately 34% by 2050 (122). In Sweden (2014) mean life expectancy was 84 years for women and 80 for men, and is estimate to increase to 89 for women and 87 for men by 2060 (123). In this thesis the term older will be used to refer to those aged ≥ 70 years. The consequences of ageing differ from one individual to another but ageing includes more or less disabilities and losses. Older people are more vulnerable to diseases as aging always involves reduced organ-function capacity (124, 125).

Feeling old is not always consistent with chronological age but it seems to be consistent with physical changes and losses (126). For example, retaining the ability to walk is essential and if you are unable to walk, the use of a walking aid can make you feel confident and independent. But, a walking aid can also be associated with an undesirable image of old age, feeling vulnerable, dependent and being forced to change one's self-image (127). Maintaining control over everyday life is important in order to experience health (128).

Mental health is a concern and might be the most frequent cause of emotional suffering and reduced quality of life among older people (129). Depression seems to be associated with age-related changes in life (130). In older people depression is often present in comorbidity with organic diseases which may mask the depressive symptoms (131). A review reported that depression is common, often persistent and seems to be unrecognized and untreated in people with cardiac diseases (132). The prevalence of depression in patients undergoing cardiac surgery is 12-23% preoperatively and 34-43% postoperatively (133-135). In a study among the very old (≥85) depressive disorders seems to be chronic and malignant. Hypertension as well as a history of stroke appears to be important risk factors for depression among very old people (136).

Dementia

As a natural process our brain mass decreases as we get older and changes occur in cognitive function (137). Such cognitive changes vary between individuals (138). Changes not part of the normal aging process are classified as neurocognitive disorders (NCD) (10) and categorized as mild neurocognitive disorders or mild cognitive impairment (MCI) and major neurocognitive disorders (dementia) (10, 139). MCI refers to changes in one or more cognitive domains or changes in memory that are not normal for an individual's age and level of education and do not meet the criteria for dementia (10 p 607).

Dementia is usually a progressive disease which includes deterioration in memory, thinking, and behaviour leading to reduced abilities to perform everyday activities. It is associated with increased mortality (140). At the beginning of the 1980s dementia was described as "the silent epidemic" (141). Today, approximately 50 million people worldwide are affected by dementia. It is estimated that the number of people living with dementia will increase to 75 million in 2030 and triple to 150 million by year 2050 (142).

Dementia develops as a consequence of a large number of mechanisms. Vascular diseases and/or specific changes in brain tissue lead, to persistent neurodegeneration. The most common cause is primary degenerative diseases (PDDs), damage of neurons (143). The deterioration in cognitive abilities related to PDDs seem to be slow and most commonly attributed to Alzheimer's disease (AD) (144-146); followed by dementia with Lewy bodies (DLB) and Parkinson's disease dementia. Dementia caused by vascular diseases, involves a reduced oxygen supply to the brain. Often, a mixed form of dementia is present. In Sweden during the period 2000 to 2012, the most common type of dementia in patients with cardiovascular diseases was AD (32%) followed by unspecified dementia (19%), vascular dementia (19%), mixed dementia (19%) (144).

The prevalence of dementia varies in Europe both between countries (147) and within countries, as is the case in Sweden (148, 149). A study from Stockholm showed a tendency to a reduced prevalence of dementia from the late 1980s to the early 2000s and an increased survival among people with dementia (148). On the other hand, in northern Sweden a population-based study among the very old (≥85 years) reported that the prevalence of dementia increased over a five year period from 26% to 37% (149).

Reported risk factors for dementia are: old age (145, 150), hypertension (151, 152), diabetes (153), stroke (154), heart failure (146), MCI (155, 156), depression (157-160) and delirium (161, 162). Studies have shown an association between anaesthesia, surgery and Alzheimer diseases but the results are inconsistent and more research is needed (163, 164). As shown, many risk factors for dementia derive from the cardiovascular system. Studies show that dementia is significant (25-40%) in older patients (≥ 70 years) admitted to emergency units but it is often missed and therefore under-diagnosed (150, 165).

Rationale for the thesis

Delirium is common after cardiac surgery and associated with complications. The incidence of PODCS will probably increase as older patients are accepted for cardiac surgery. The causative mechanism of PODCS is not fully understood, and there seems to be a lack of knowledge about potential predisposing and precipitating risk factors behind PODCS in older people. Long-lasting consequences of PODCS such as the development of dementia are scarcely investigated. There is also limited research concerning patients' experiences of undergoing cardiac surgery and how it might affect them in the long term. However, delirium is difficult to detect in the caring environment without a screening instrument. Today there are easy-to-use assessment scales but they are not validated in older patients undergoing cardiac surgery.

Aims

Overall aim

The overall aim of this thesis was to investigate postoperative delirium in older people undergoing cardiac surgery with CPB; focusing on risk factors, dementia and patients' experiences, and to evaluate an assessment for screening delirium.

Specific aims

The specific aims of the studies were;

1) To identify potential predisposing and precipitating risk factors behind delirium in consecutive patients, 70 years and older undergoing cardiac surgery.

2) To investigate whether postoperative delirium was associated with the development of dementia within 5 years after cardiac surgery in patients aged ≥ 70 years.

3) To illuminate experiences of undergoing cardiac surgery among older people diagnosed with postoperative delirium, a one year follow-up.

4) To evaluate the Swedish version of Nu-DESC as a screening tool for nurses to use in detecting postoperative delirium in patients 70 years and older undergoing cardiac surgery.

Materials and methods

This thesis is based on a cohort study and applied both qualitative and quantitative methods. A schematic overview of the studies (I-IV) is presented in table 2.

Table 2. Overview of the studies I-IV.

Study/Design	Year	Participants	Data collection	Analysis
I Cohort study (published 2013)	2009	n=142 mean age 76.6 females 35.2%	MMSE, OBS, GDS, KATZ-ADL, NRS-pain	Quantitative Multivariable logistic regression
II Longitudinal cohort study (manuscript)	2009-2014	n=114 mean age76.5 females 30.7%	MMSE, OBS, GDS, KATZ-ADL, NRS-pain	Quantitative Descriptive statistics, Multivariable logistic regression
III Interviews (published 2015)	2010	n=49 mean age 78.9 females 34.6%	Semistructured interviews	Qualitativ Content analysis
IV Cohort study (published 2013)	2009	n=142 mean age 76.6 females 35.2%	MMSE, OBS, Nu-DESC, GDS, KATZ-ADL, NRS-pain	Quantitative Descriptive statistics

MMSE: mini-mental state examination; OBS: organic brain syndrome scale; Nu-DESC: nursing delirium screening scale; GDS-15: geriatric depression scale; Katz ADL:katz staircase including the katz ADL index; NRS: numeric rating scale of pain

Participants and settings:

All participants included were scheduled for routine cardiac surgery with CPB at the Cardiothoracic Surgery Department (CSD), Heart Centre, Umeå University Hospital, Sweden, between February and October 2009. During that period data were collected for studies I, II and IV. Three follow-ups were conducted during 2010 (II, III), 2012 and 2014 (II).

Cardiothoracic surgery department and Care

The University Hospital is a regional hospital for the Northern Health Care Region covering approximately 50% of the area of Sweden, and encompasses the County Councils in Norrbotten, Västerbotten, Västernorrland and Jämtland (Figure 1). The region has three county hospitals, eight general hospitals and approximately 900,000 inhabitants (166). This implies long journeys for many patients admitted to the CSD. Both elective and acute cardiac surgery procedures are performed in the CSD.

Figure 1. Map of Sweden and the Northern Health Care Region modified after County Council of Västerbotten, Life and Health in Västerbotten 2015 (166).

The CSD Heart Centre Umeå is organized in four units (general ward, operating room, intensive care unit (ICU) and step-down unit). The cardiac surgery units comprise mostly four-bed rooms but single rooms are also available. During their hospital stay patients pass through five different units (general ward, operating room, ICU, step-down unit and general ward again). The healthcare professionals working in the units at the time of studies (2009) were as described below. In the general ward registered nurses (RN) and enrolled nurses (EN), one RN and one EN, working together as a pair responsible for approximately six patients. In the operating room two RNs specialized in operating room nursing (ORNs), one RN specialized in anaesthetics nursing (nurse anaesthetist), one RN specialized in cardiac vascular perfusion (perfusionist), two physicians specialized or trained in cardiac surgery (cardiac surgeons) and one physician specialized or trained in anaesthetics, perioperative medicine and intensive care (anaesthesiologist) were responsible for one patient at a time. In the ICU one RN specialized in intensive care (ICU nurse) was responsible for one patient at a time, and in the step-down unit most of the time one RN was responsible for two patients. Cardiac surgeons and anaesthesiologists were also responsible for patients in the general ward, ICU and step-down unit. There were also physiotherapists working in the CSD.

In general, patients were admitted to the CSD general ward two days before surgery. They received information about the surgical procedure, routines and the nursing care. Several professions were involved in the information procedure. Additional assessments and tests were carried out when needed (e.g echocardiography, x-ray, angiography, and laboratory testing).

The preoperative and perioperative care and procedures in 2009 are described below. Two hours before surgery patients received premedication with oral oxycodone, acetaminophen, and zopiclone. Approximately 30 min before arriving in the operating room intramuscular morphine and, in a few cases, ketobemidone or morfine-scopolamine were administered. General anaesthesia was induced intravenously with propofol, fentanyl, and pancuronium, with or without a small dose of midazolam. Anaesthesia was maintained with isoflurane in air and oxygen and additional fentanyl. Blood pressure was controlled by means of crystalloid transfusion and vasoactive medication (norepinephrine or phenylephrine). Intra-arterial blood pressure was documented manually every 5 minutes during surgery, and every 15:th to 30:th minute postoperatively. The need for crystalloid and blood transfusion was assessed by detailed monitoring of hemodynamics, blood-gas measurements, urine output and echocardiographic findings. Surgery was performed according to standard methods, including cardioplegic arrest during aortic cross clamping. CPBs were conducted using the alphastat regimen and non-pulsatile blood flow at a rate sufficient to maintain the venous oxygen saturation >75%. Infusions made during CPBs were crystalloid in type. Blood pressure was adjusted to keep mean arterial blood pressure above 50 mmHg. Body temperature was lowered to 34 °C and actively increased to 37 °C before weaning from the CPB. Isoflurane was administered throughout the CPB procedure, supplemented with propofol at the start of rewarming the patient and weaning in the ICU. In the first postoperative hours (approximately >24 hours), patients were cared for in the ICU. When they were stable regarding respiration and circulation they were extubated. If complications occur, the ICU stay is extended. On day one postoperatively, after extubation, patients usually received care in the step-down unit; for some the stay could be longer. If vital signs were stable they were moved to the general ward, usually on day three postoperatively. Patient's vital signs determined the level of care and if necessary their relocation to the ICU or step-down unit. Postoperative pain relief during the period of hospitalization generally comprised oral paracetamol and oxycodone, with incremental doses intravenously of ketobemidone when needed. Patients with disturbances and behaviour changes that affected patients' care were generally relocated to the step-down unit or the ICU. Patients with hyperactive PODCS were generally treated with oral klometiazol or ziprasidon, orally or intravenously administered haloperidol and, when needed, propofol infusion.

Participants

In this thesis I will refer to those who participated as patients in studies I and IV and as participants in studies II and III (fig 2 flow chart).

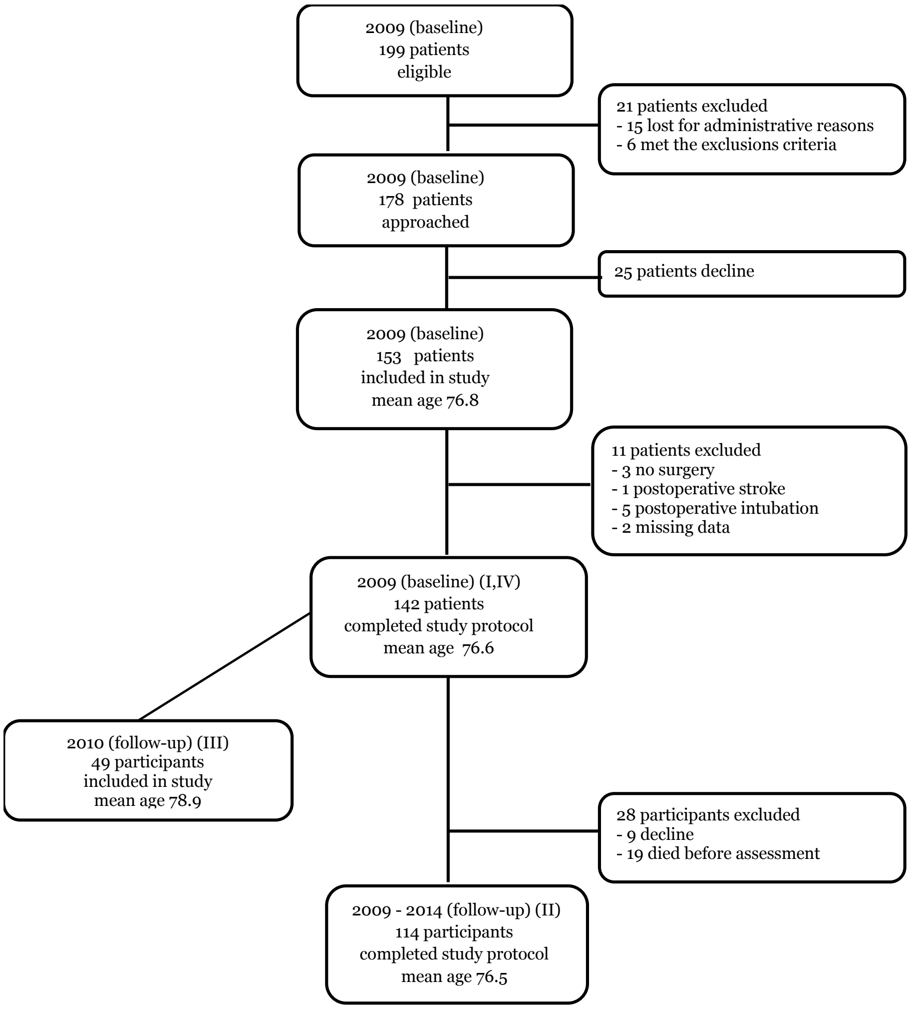

Figure 2. Flow chart for the patients/participants who were admitted to the Cardiothoracic Surgery Department and included in all four studies, I-IV

Studies I and IV

During the study period in 2009 199 patients were consecutively accepted as eligible for inclusion. The inclusion criteria were age ≥ 70 years and being scheduled for routine cardiac surgery with CPB. The cardiac surgery procedures included CABG, aortic valve with and without procedures involving the ascending aorta, mitral valve, or combinations thereof. Exclusion criteria were operation within 24 hours of admission (acute procedures), documented psychiatric disease or dementia, severe visual or hearing problems and not fluent in Swedish. For administrative reasons 15 potential participants were not included. Six patients met the exclusion criteria. In total, 178 patients were asked to participate and 25 declined. A total of 153 agreed to participate and 11 patients were lost for a variety of reasons. A total of 142 patients completed the study protocol and are included in studies I and IV (Table 3). The 36 patients not included did not differ from the cohort in terms of age, sex and cardiac surgery procedures.

Table 3. Baseline characteristics in patients included in studies I and IV.

Parameter	All patients (*n* =142)	Parameter	All patients (*n* =142)
Predisposing variables		*Predisposing variables*	
Preoperative variables	Mean SD (%)	Preoperative variables	Mean SD (%)
Age (year)	76.6 ± 4.4	Hypertension	83.8
Sex (female)	35.2	NYHA(class IV)	17.6
Height	169.1 ± 9.2	SAP (mmHg)	139.4 ± 20.8
Weight (kg)	75.7 ± 13.5	DAP (mmHg)	75.1 ± 10.3
BMI	26.4 ± 4.2	Pulse type (not SR)	7.8
Impaired vision (glasses)	92.3	Oxygen saturation periferal (%)	96.7 ± 2.0
Impaired hearing (hearing device)	21.8	Temp	36.5 ± 0.3
I-ADL dependent	38.7	Angina	29.8
P-ADL dependent	3.5	Myocardial infarction(previous)	40.4
Living alone	38.7	Left ventricular function (reduced)	32.4
Education (≥7 year)[1]	46.5	Previous cardiac surgery	5.7
MMSE score (0-30)	27.0 ± 2.6	Previous PCI	14.8
NRS pain (0-10)[1]	1.8 ± 2.1	Platelet inhibitor	82.4
GDS-15 score (0-15)	2.5 ± 2.2		
Depression	14.8		
Diabetes	16.2		
Cerebrovascular history	14.8		
Gastric /peptic ulcer	12.0		
Malignant disease	3.5		

BMI:body mass index; I-ADL:instrumental activities of daily living; P-ADL:personal activities of daily living; MMSE:mini-mental state examination; NRS:numeric rating scale of pain; GDS-15:geriatric depression scale
NYHA:new york heart association functional classification;
SAP:systolic arterial blood pressure; DAP:diastolic blood pressure; PCI:percutaneous coronary intervention;
[1]NRS pain: n= 140 [1]Education (≥7 year) n=139

Study II

During 2009 142 participants completed the assessments and were invited to three follow ups after surgery at one, three and five year. Inclusion for study II was that the follow ups required that necessary assessments (for cognition, depression, delirium and physical activities) were completed to ascertain a dementia diagnosis. In total 28 participants were excluded, 19 died before completion of necessary assessments during the follow-up period, 9 declined to participate further during the follow-ups. Participants not included (n=28) were comparable to the final sample with respect to age, education, MMSE-score, depression, and proportion of patients who developed PODCS. The proportion of participants with severe heart failure as well as proportion of women was lager in the excluded group. The final study sample comprised 114 participants. Baseline characteristics of the participants included in study II are shown in Table 4.

Table 4. Baseline characteristics, including preoperative, operative and postoperative variables, of participants included in study II.

Parameter	All Participants (*n* =114)	Parameter	All Participants (n=114)
Preoperative variables	Mean SD (%)	Operative and postoperative variables	Mean SD (%)
Age (year)	76.5 ± 4.4	CABG isolated	58.8
Sex (female)	30.7	Valve procedures isolated	20.2
BMI	26.6 ± 3.9	Combined procedures	21.1
Impaired vision (glasses)	91.2	Operation time (h)	2.9 ± 0.9
Impaired hearing (hearing device)	23.7	CPB time (h)	1.4 ± 0.6
Living with partner	61.4	Ventilator time (h)	6.9 ± 3.3
I-ADL dependent	34.2	ICU time (h)	22.3 ± 19.4
P-ADL dependent	3.5	PODCS	56.1
Education (≥7 year)	47.4	Milrinone or Levosimendan required [2]	28.3
MMSE score (0-30)	27.0 ± 2.8	Blood loss (l)	0.4 ± 0.4
MMSE score (≤ 24)	7.9	Volume load, blood excluded (l)	3.8 ± 1.1
NRS pain (0-10) [1]	1.7 ± 2.0		
GDS score (0-15)	2.3 ± 2.0		
Depression	12.3		
Diabetes	16.7		
Cerebrovascular history	14.9		
Myocardial infarction (previous)	40.4		
NYHA I (class)	3.5		
NYHA II (class)	27.2		
NYHA III (class)	57.9		
NYHA IV (class)	11.4		
SAP mmHg	139.5 ± 21.2		
DAP mmHg	75.2 ± 10.3		
Number of drugs prescribed	5.7 ± 2.4		
Antikoagulans	87.7		
B-blockers	71.9		
Calcium channel blockers	28.1		
Antilipemic agents	69.3		
Antidepressants	5.3		
Diuretics	36.8		
RAAS -blockers	58.8		

BMI:body mass index; I-ADL:instrumental activities of daily living; P-ADL:personal activities of daily living; MMSE:mini-mental state examination; NRS:numeric rating scale of pain; GDS-15:geriatric depression scale; NYHA:new york heart association functional classification; SAP:systolic arterial blood pressure; DAP:diastolic blood pressure; CABG:coronary artery bypass grafting; CPB:cardiopulmonary bypass; ICU: intensive care unit; PODCS: postoperative delirium; RASS:renin-angoitensin-aldosterone system; Combine procedures: combination of coronary artery bypasses and/ or valve surgery and/or intervention of the ascending aorta;

[1] NRS pain: n= 113 one missing variabel no dementia,

[2] Milrinone or Levosimendan required n=113 one variabel missing variable no dementia.

Study III

Study III, was based on a convenience sample from the 142 included in studies I and IV, and comprised 49 participants, 32 men and 17 women (median age 78, range 71-91 years). The inclusion criterion was diagnosis of PODCS according to DSM-IV-TR. They all managed their daily living, and 45% were living alone.

Procedure

A power analysis was performed before study IV began to determine the required number of patients, as outlined by the conditions described in that study.

The author and one RN collected data for all the studies (I, II, III and IV). They both worked at the cardiothoracic department, one as an anaesthetic nurse (author) and one as a RN on the general ward. In preparation for the data collection they received special training in both delirium assessments and the use of other assessments scales. The training included auscultation with a RN specialized in geriatrics and experienced in POD. Before the data collection started in 2009, the data collectors were tested for consistency in their assessments. The special training also included education in geriatric assessments and treatments.

Before study IV began the nursing staff, RNs and ENs, in the CSDs three sections participated in a one-hour introductory session. The session included the use of Nu-DESC and extended the knowledge of delirium. In total, 53 (50%) out of 105 nurses (RN n=93 and EN n=12) received this information. In addition, folders containing information about delirium, its symptoms and underlying causes (predisposing and precipitation factors) together with a quick reference guide to the Nu-DESC were made available to all staff during the study. In addition a two-week pre-study phase was conducted to train the nursing staff in the use of Nu-DESC. The nursing staff observed and screened participants for PODCS using Nu-DESC after extubation up to discharge. The Nu-DESC was an integrated part of the patient´s digitalized medical record. Registrations were made three times daily at the end of each work-shift. The data collectors were blinded to the Nu-DESC results during the data collection (IV).

Data collection

In this thesis face to face structured interviews were conducted. A protocol included different assessments scales (I, II, IV) are presented in table 5.

Semi-structured interviews were performed during home visits (III). The structured interviews included demographics, social function, coexisting medical conditions, medication, as well as cognitive and physical functions. Additional data were also retrieved from the local clinical database, the medical records, and nursing staff during hospital stay (I, II, IV). During the follow-ups sometimes next of kin as well health care professionals were interviewed (II). The interviews during hospital stay lasted approximately 25-45 minutes and home-visits about two hours.

Studies I and IV

Data were collected in the CSD (2009) and the first structured interview was carried out before surgery, on the general ward (timepoint 1). The second interview was performed after surgery, after extubation (+1 day, timepoint 2) in the ICU, or, for the majority of the participants, in the step-down unit. The third interview was performed on day four (± 1 day, timepoint 3) mainly on the general ward but sometimes in the step-down unit or the ICU (Table 5).

Study II

In study II, data collections were conducted at the CSD during 2009, and included home interviews carried out during three follow-ups, one year (± 3 months, timepoint 4), three years (± 6 months, timepoint 5) and five years (± 6 months, timepoint 6) after surgery. The protocol was used in the same chronological order in all data collections (Table 5). The intention was for the data collectors to follow the same participant, but this proved impossible in some cases. During the follow-ups the majority of the participants were living independently, with only a few in residential care facilities.

Study III

In study III, semi-structured interviews were conducted one year after cardiac surgery. Data collection was conducted as part of the longitudinal cohort study, and took place in the participants' homes. The interviews started with the qualitative interview and then moved on to the remaining assessments. The first open question was "Please, tell me how you experienced your hospitalization?" Follow-up questions were also asked to encourage participants to share their feelings and experiences and to facilitate talking about them. The topics included experiences or memories of preoperative information, the first postoperative days, dreams or visions, being confused, and thoughts and feelings the participants did not usually have. The interviews were audio-recorded and lasted between 9 and 32 minutes (mean =18 minutes). Only those who were diagnosed with PODCS were included in the analysis.

Assessments scales and Diagnoses

The assessments scales used are presented in the following section. An overview of the assessments in the studies is presented in Table 5.

Table 5. Assessment scales used in the four studies.

Assessment scales	2009 Preop	2009 Postop day 1	2009 Postop day 4	2010 Follow-up 1 year	2012 Follow-up 3 year	2014 Follow-up 5 year
MMSE	x	x	x	x	x	x
OBS	x	x	x	x	x	x
Nu-DESC		xxx	xxx			
GDS-15	x	x	x	x	x	x
KATZ ADL	x		x	x	x	x
NRS pain	x	x	x	x	x	x

Preop: preoperative; Postop:postoperative; Nu-DESC:nursing delirium screening scale; MMSE:mini-mental state examination; OBS:organic brain syndrome scale; GDS-15:geriatric depression scale; Katz ADL:katz staircase including the katz ADL index; NRS: numeric rating scale of pain

The Mini-Mental State Examination

The Mini-Mental State Examination (MMSE) was developed as a screening test to assess global cognitive function, including orientation in time and space, naming, recall, attention, language, visual constructional abilities (167) as well as changes and cognitive decline over time (168). The scores range from 0 to 30 and the severity of cognitive impairment is classified into three levels, 30-24= no impairment; 23-18 mild impairment; and 17-0 severe impairment (168). The MMSE is sometimes used in research as part of an assessment for delirium (2, 15, 37). The MMSE was dichotomized < 24 indicating a reduced brain reserve capacity.

In study II for some participants the MMSE was administered over the telephone (167). It has been shown that telephone versus face-to-face MMSE interviews correlate strongly r = 0.85 (169). The total MMSE score that could be obtained through a telephone interview was 22 p c.f Roccaforte (169). The scores the participant received were divided by 22 and multiplied by 30 to give as comparable a score as possible. This was performed for four participants once in year five and one participant three times in study II.

The Organic Brain Syndrome Scale (OBS)

The Organic Brain Syndrome Scale (OBS) was developed to assess clinical manifestations of the various psychiatric symptoms that appear in cases of delirium, dementia and other organic brain disorders, among young and older people (66, 170). The scale includes clinical symptoms such as:

different time-related variations and fluctuations of the clinical state; emotional reactions; suspiciousness; hallucinations; paranoid symptoms and delusion. It also includes language and speech disturbances; neurological symptoms; spatial orientation and recognition and practical ability of the clinical state useful for diagnosis according to the DSM criteria for different psychiatric symptoms. The OBS consists of two parts, the disorientation subscale (15 items) measuring awareness and orientation, and the confusion subscale (39 items), which is an observation scale concerned with variations in clinical state, as described above. Each item is scored from 0 to 3, where 0 indicates lack of any symptoms and 3 indicates strong manifestation (170, 171). OBS is a combined interview and observation scale and covers both reported symptoms and signs observed by care providers and next of kin as well as observations and interviews. The scale has been validated in older people with dementia (170) as well as older people (> 65 years) undergoing cardiac surgery (15) and met the DSM-IV criteria for delirium (9). In this thesis OBS was modified with a total of 34 items being used. The disorientation subscale measures similar areas to the MMSE and was disregarded as were the ADL items as the participants were assessed using the Katz ADL index. The information gathered with the OBS scale was used to help assess delirium symptoms, depressive symptoms and dementia.

The Nursing Delirium Screening Scale (Nu-DESC)

The Nursing Delirium Screening Scale (Nu-DESC) was developed as a fast, systematic screening scale for assessing delirium. Nu-DESC was developed for clinical routine care for nurses, since they work closely, around-the clock with the patients (78). It was based on the Confusion Rating Scale (CRS) (172), but in addition to the four items in CRS, a fifth item was added to screen for psychomotor retardation (hypoactive delirium), since it is frequently present in delirium psychomotoric subtypes (78). For study IV, the Nu-DESC scale was translated from English into Swedish with the permission of its creator, Jean-David Gaudreau. It was translated according to procedural principles for translation (173).

Nu-DESC is an observation scale and does not need patient participation. The scale was developed to have a high sensitivity for delirium symptoms and is based on five items: disorientation, inappropriate behaviour, inappropriate communication, illusions or hallucinations and psychomotor retardation. The five items are graded from 0–2, with 0 denoting no symptom, 1 the symptom is present but in a mild form and 2 the symptom is present and apparent. The scale has a maximum possible score of 10, indicating a more severe delirium; a total score ≥ 2 is required to meet the criteria for a diagnosis of delirium. The face validity was tested and rated high when each item assessed the feature of delirium and the overall concept according to DSM-IV (78). The Nu-DESC showed a sensitivity of 85.7% and a specificity of 86.8% when it was used in a hemato-oncology/internal medicine unit (78). Nu-DESC has been shown to have high agreement with DSM-IV and to be valid and reliable in detecting delirium in various settings (sensitivity/specificity); recovery room (95%/ 87%) (39), surgical ward (98%/ 92%) (80). Nu-DESC interrater reliability was shown to be 0.83 (80).

The Geriatric Depression Scale-15 (GDS-15)

The Geriatric Depression Scale-15 (GDS-15) was developed to assess depressive symptoms. The GDS-15 scale has "yes" or "no" questions and has a range of 0-15 with higher scores (≥ 5) indicating more depressive symptoms and increased risk of depression (174-176). The GDS scale is considered a valid scale for measuring depressive symptoms among older people with stroke (177) and very old people with and without cognitive impairment (MMSE score ≥10) (178).

The Katz Staircase including the Katz ADL index

The Katz Staircase including the Katz ADL index was developed to assess participants' functional status and need for assistance in activities of daily life (179, 180). The scale includes both Personal-ADL (P-ADL) – i.e. a person's basic capacity to care for him/herself (dressing, toileting, bathing, transfer, continence and feeding) and Instrumental-ADL (I-ADL) – the ability to perform household chores (cleaning, shopping, transportation and cooking). In this thesis I-ADL and P-ADL were assigned and dichotomized to independent or dependent.

The Numeric Rating Scale (NRS pain)

The Numeric Rating Scale (NRS pain) was developed to assess pain intensity. It is an 11-point visual analogue scale (VAS), ranging from 0 (no pain at all) to 10 (most severe pain imaginable) (181). The NRS has proved to be applicable for assessment of pain in many different settings (182).

Diagnoses of delirium, depression and dementia

The diagnosis of PODCS was set after the data collection in 2010 by two experienced researchers (one nurse and one physician) specializing in geriatric medicine. They analysed the MMSE and OBS scale independently in three steps: in step one MMSE was analysed; in step two the OBS scale was analysed; step three combined analyses of the OBS scale and MMSE scale were conducted. Finally, the two researchers reached consensus on the diagnoses for PODCS (DSM-IV-TR) (9). Dementia and depression diagnoses were set according to DSM-IV-TR after completion of the longitudinal cohort study. The same physician reviewed and evaluated the collected assessments and interviews from 2009 to 2014 (MMSE, OBS-scale, GDS-15, Katz-ADL, medication). Ongoing medical treatments with antidepressants were considered an indication of depression.

Analysis

Study I

In Study I, descriptive statistics were used to present the patients´ characteristics before surgery and during their hospital stay. Preoperative variables (predisposing factors) and operative and intra- and early postoperative periods within 24 hours after surgery variables (precipitating factors) were reviewed for normality, dependencies and outliers. Comparisons between groups (with PODCS and without PODCS) were made by using t-test and Chi-square. Continuous variables were used in their numeric mode and were presented with mean and standard deviation (SD), categorical data were presented as numbers and percentages. A variable with obvious co-variability, only one was selected of its assumed higher clinical relevance. The inclusions in multivariable testing were means of univariate logistic regression, and were restricted to variables associated with PODCS and a *p*-value of < 0.10. Adjustment was made for age and sex in the multiple logistic regression analysis was used.

The univariate regression analyses were used to estimate the association between PODCS as the dependent variable and the predisposing and precipitating variables as independent variables. The multivariate logistic regression followed a manual backward conditional approach. First predisposing and precipitating variables were analysed separately in two multivariable models excluding the independent variables one at a time until only independent variables with a *p*-value <0.05 were remained in the models. Finally, a combined multivariable model was conducted, including all final predisposing and precipitating variables. Difference were considered statistically significant if $p < 0.05$. Data were tabulated in Excel for overview and The Statistical Package for Social Sciences version 18 (IBM SPSS Statistics, IBM, Inc., Chicago, IL, USA) was used for statistical calculation.

Study II

In Study II, descriptive statistics were used to present the patients´ baseline characteristics and separated into preoperative variables and operative and postoperative variables. Means were used to describe the change in MMSE scores over six timepoints (preoperatively, postoperatively day one, day four, and follow-ups in 2010, 2012 and 2014). Differences between participants (with or without dementia or with or without PODCS) where investigated using independent samples t-test on each occasion and paired samples t-test was used to investigate the decline in MMSE-score over time.

Univariate logistic regression analyses were used followed by a multivariable logistic regression to estimate the association between dementia as the dependent variable and the preoperative variables and operative and postoperative variables as independent variables. The inclusions in multivariable testing were means of univariate logistic regression, and were restricted to variables associated with dementia and a *p*-value of < 0.10. First, two separate multivariable models were constructed ; preoperative and operative together with postoperative variables were analysed in backward estimation procedures excluding the independent variables one at a time until only independent variables with a p-value below 0.05 were remained in the models. As a final step, a combined multivariable model was conducted, including all final variables from the two separate models. A *p*-value of < 0.05 was considered statistically significant. The results in the logistic regressions models were presented as odds ratio (OR) with 95% confidence intervals (CI). All analyses were performed using SPSS software (version 21.0 for Windows; IBM, Armonk, NY, USA).

Study III

Study III comprised semi-structured interviews which were transcribed verbatim. The interviews varied, some were rich some were fragmented. Qualitative content analysis was used to systematically analyse data (183). The analysis involves several steps to identify differences and similarities in a text. The text was analysed according to the steps described by Graneheim and Lundman (184). The first step was to read through the transcribed interviews to gain a sense of the whole. In the second step, the text was divided into meaning units, words or sentences related to each other by their content and context. In the third step meaning units were condensed while ensuring that the core meaning was retained, and labelled with a code. In the last step the codes were sorted into eleven sub-themes, and then abstracted into four themes. Finally, the text was compiled into a description of the content in the interviews. Qualitative content analysis involves moving back and forth between transcribed text, meaning units, codes, sub-themes and themes. All the authors discussed every step in the analysis process until consensus was achieved.

Study IV

In Study IV, the Nu-DESC score was validated against assessments using the MMSE and the OBS-scale based on DSM-IV-TR criteria for delirium (9). Descriptive statistics were used and presented as separate groups for participants with and without PODCS. Normality of continuous variables was analysed. Non-parametric statistics were applied using the Mann-Whitney U-test, Pearson´s Chi^2 test and Fisher´s exact test. Binominal comparison between PODCS assessment methods was analysed using the McNemar test. Sensitivity and specificity between the methods were analysed. A p-value of < 0.05 was considered as significant. Data were tabulated in Excel for overview and The Statistical Package for Social Sciences version 18(IBM SPSS Statistics, IBM, Inc., Chicago, IL, USA).

Ethics

All studies are based on the ethical principles as manifested in the Declaration of Helsinki (185) and approved by the Regional Ethical Review Board in Umeå, Sweden (Dnr 08-169M, Dnr 2010-34-32, Dnr 2011-315-32M, Dnr, 2014-107-32M). Participants received written and oral information about the aim of the study preoperatively, at the hospital close to the time for surgery (2009). They were also informed by letter and received oral information by telephone before the three follow-ups (2010, 2012, and 2014). Participation was voluntary and the participants were assured of confidentiality. They were informed that participation in the study did not interfere with their clinical care and treatments and they could withdraw and cancel participation at any time without giving any reason. Their written informed consent was obtained (2009-2014) and when participants could not give this it was obtained from their next of kin. When needed the next of kin or member of staff in residential care was invited to be present during the interview, in order to support and interpret the situation (cf 186). Data gathered from these four studies are kept and stored in a secure manner to prevent unauthorized access. The results are displayed on a group level; no individuals can be identified in the results.

Results

The presentation of the results in my thesis is based on the main findings in each study - I, II, III and IV.

Study I

Study I, the incidence of PODCS was 54.9% (78/142). Tables 6 and 7 describe the univariate results with respect to PODCS. Potential risk factors independently associated with PODCS were identified in the final multivariable model as: age, diabetes, gastritis/ peptic ulcer, increased volume load during operation (blood excluded), increased ventilator time in the ICU, highest temperature recorded while in the ICU, and a higher plasma sodium concentration while in the ICU. When predisposing and precipitating factors were combined, the predictive strength of the model improved (Table 8).

Table 6. Patients' characteristics for predisposing variables and univariate results included in Study I.

Parameter	All patients (*n* =142) Mean SD (%)	No Delirium (*n* =64) Mean SD (%)	Delirium (*n* =78) Mean SD (%)	Univariate *p* -value
Predisposing				
Preoperative				
Age (year)	76.6 ± 4.4	75.9 ± 4.2	77.2 ± 4.5	0.092 [a]
Sex (female)	35.2	40.6	30.8	0.222 [b]
Weight (kg)	75.7 ± 13.5	72.3 ± 11.8	78.4 ± 14.3	0.009 [a]
BMI	26.4 ± 4.2	25.5 ± 4.0	27.1 ± 4.2	0.031 [c]
Impaired vision (glasses)	92.3	90.6	93.6	0.51
Impaired hearing (hearing device)	21.8	18.8	24.4	0.42
Education (≥7 year)[2]	46.5	50.8	44.7	0.48
NRS pain[1]	1.8 ± 2.1	1.4 ± 1.8	2.2 ± 2.2	0.030 [a]
Type of accommodation (own house)	56.3	62.5	51.3	0.18
Living alone	38.7	37.5	39.7	0.78
I-ADL dependent	38.7	0.3	0.4	0.19
P-ADL dependent	3.5	3.1	3.8	0.82
MMSE score (0-30)	27.0 ± 2.6	27.3 ± 2.2	26.7 ± 2.9	0.18
GDS-15 score (0-15)	2.5 ± 2.2	2.3 ± 2.2	2.7 ± 2.2	0.26
Depression	14.8	10.9	17.9	0.24
Cerebrovascular history	14.8	12.5	16.7	0.49
Hypertension	83.8	85.9	82.1	0.53
NYHA (class IV)	17.6	12.5	21.8	0.15
Angina	29.8	29.7	29.9	0.98
Myocardial infarction(previous)	40.4	42.2	39.0	0.70
Left ventricular function (reduced)	32.4	26.6	37.2	0.18
Previous cardiac surgery	5.7	6.3	5.1	0.76
Previous PCI	14.8	10.9	17.9	0.25
Diabetes	16.2	9.4	21.8	0.052 [a]
Gastritis /peptic ulcer	12.0	6.3	16.7	0.067 [a]
Malignant disease	3.5	4.7	2.6	0.50
SAP (mmHg)	139.4 ± 20.8	140.2 ± 21.0	138.7 ± 20.8	0.66
DAP (mmHg)	75.1 ± 10.3	76.0 ± 9.9	74.3 ± 10.6	0.32
Pulse type (not SR)	7.8	9.4	6.5	0.53
Oxygen saturation periferal (%)	96.7 ± 2.0	97.0 ± 1.6	96.4 ± 2.3	0.053 [a]
Hemoglobin (g/l)	135.6 ± 12.6	136.0 ± 11.6	135.3 ± 13.4	0.78
Sodium concentration/plasma (mmol/l)	139.5 ± 2.4	139.3 ± 2.3	139.7 ± 2.5	0.33
Potassium concentration/plasma (mmol/l)	4.3 ± 0.3	4.3 ± 0.3	4.3 ± 0.3	0.57
Platelet count (10^9/L)	225.6 ± 55.4	234.3 ± 57.2	218.5 ± 53.3	0.096 [a]
CABG isolated	59.9	67.2	53.8	0.11
Valve procedures isolated	19.7	20.3	19.2	0.87
Combined procedures	20.4	12.5	26.9	0.038 [a]

[a] Denotes variables tested in the multivariable models, with a P-value of <0.10.

[b] Denotes variables added at multivariable testing due to their expected principal importance rather than their statistical influence at univariate testing.

[c] Denotes variables (P-value <0.10) avoided in the multivariable models because of covariability aginst other used parameter.

BMI:body mass index; NRS:numeric rating scale of pain; I-ADL:instrumental-activities of daily living; P-ADL:personal-activities of daily living; MMSE:mini-mental state examination; GDS-15:geriatric depression scale; NYHA:new york heart association functional classification; PCI:percutaneous coronary intervention; SAP:systolic arterial blood pressure; DAP:diastolic blood pressure; CABG:coronary artery bypasses grafting; Combine procedures: combination of coronary artery bypasses and/or valve surgery and /or intervention of the ascending aorta;

[1] NRS pain: n= 140 two missing variable in delrirum,

[2] Education (≥7 year)1 n=139 one variabel missing in no delirium and two missing in delirium

p -values refer to univariate logistic regression analyses.

Table 7. Patients' characteristics for precipitating variables operative and early post-operative variables within 24 hours and univariate results included in Study I.

Parameter	All patients (n=142) Mean SD (%)	No Delirium (n=64) Mean SD (%)	Delirium (n=78) Mean SD (%)	Univariate p-value	
Precipitating					
At operation					
Operation time (h)	2.9 + 0.8	2.7 + 0.6	3.0 + 1.0	0.020	a
CPB time (h)	1.5 + 1.0	1.4 + 1.3	1.6 + 0.7	0.37	
Lowest oxygen saturation (%)	96.9 + 2.1	97.2 + 1.6	96.6 + 2.4	0.079	a
Insulin infusion required	16.7	9.5	22.7	0.045	a
Adrenalin required	10.0	12.5	7.9	0.37	
Phenylephrine required	22.9	23.4	22.4	0.88	
Norepinephrine requried	96.4	95.3	97.4	0.52	
Blood products required	12.7	7.8	16.7	0.12	
Blood loss (l)	0.5 + 0.4	0.4 + 0.3	0.5 + 0.4	0.079	a
Diuresis (l)	0.8 + 0.4	0.7 + 0.4	0.8 + 0.3	0.22	
Volume load, blood excluded (l)	3.7 + 1.0	3.4 + 0.6	4.0 + 1.3	0.003	a
In the ICU					
ICU time (h)	22.4 + 19.5	18.2 + 5.5	25.8 + 25.4	0.013	b
Ventilator time (h)	7.4 + 7.9	5.9 + 2.0	8.6 + 10.4	0.005	a
Lowest oxygen saturation (%)	94.7 + 2.1	95.1 + 2.1	94.3 + 2.0	0.021	a
Highest temperature recorded (°C)	37.1 + 0.5	37.0 + 0.5	37.2 + 0.5	0.068	a
Pulse rate	81.0 + 13.4	80.9 + 13.2	81.1 + 13.6	0.95	
Pulse type (not SR)	10.6	9.4	11.5	0.95	
Bleeding, recorded at 8 h (l)	0.5 + 0.3	0.5 + 0.3	0.5 + 0.4	0.60	
Hemoglobin, lowest recorded (g/l)	95.0 + 11.1	96.0 + 11.4	94.2 + 10.8	0.34	
Blood products required	33.8	29.7	37.2	0.35	
Sodium concentration /plasma (mmol/l)	138.1 + 2.4	137.6 + 2.4	138.5 + 2.4	0.03	a
Potassium concentration/ plasma (mmol/l)	4.9 + 0.4	4.9 + 0.4	4.9 + 0.3	0.88	
Creatinine concentration (mg/l)	83.0 + 24.4	81.8 + 25.9	84.1 + 23.3	0.57	
Leukocyte count (10^9/l)	10.9 + 3.3	10.8 + 3.5	11.0 + 3.1	0.75	
Hemoglobin (g/l)	104.0 + 11.5	104.6 + 13.2	103.6 + 10.1	0.61	
Platelet count (10^9/l)	162.4 + 43.3	168.3 + 41.6	157.6 + 44.3	0.14	

[a] Denotes variables tested in the multivariable models, with a P-value of <0.10.

[b] Denotes variables (P-value <0.10) avoided in the multivariable models because of covariability aginst other used parameter.

CPB:cardiopulmonary bypass; ICU: intensive care unit;
p-values refer to univariate logistic regression analyses.

Table 8. Multivariable logistic regression analyses displaying factors independently associated with PODCS in Study I.

Parameter	*p*-value	OR	CI low	CI high
Predisposing variables				
Preoperative variables				
NRS pain (0-10)	0.042	1.20	1.01	1.44
Diabetes	0.029	3.24	1.13	9.32
Oxygen saturation periferal (%)	0.045	0.82	0.67	1.00
Combined cardiac-surgery procedure	0.024	2.98	1.15	7.70
Precipitating variables				
Operative and early post-operative variables within 24 h				
At operation				
Volume load, blood excluded (l)	0.003	2.19	1.30	3.67
In ICU				
Ventilator time (h)	0.027	1.20	1.02	1.41
Sodium concentration/plasma (mmol/l)	0.043	1.17	1.00	1.37
Predisposing variables and precipitating variables				
Combined model including predisposing and precipitating factors				
Age (year)	0.036	1.10	1.01	1.21
Diabetes	0.032	3.49	1.11	10.99
Gastritis /peptic ulcer	0.050	4.00	1.00	16.06
Volume load at op (blood excluded) (l)	0.001	2.77	1.51	5.11
Ventilator time ICU (h)	0.042	1.20	1.01	1.42
Highest temperature recorded in ICU (°C)	0.044	2.23	1.02	4.85
Sodium concentration/plasma (mmol/l) in ICU	0.038	1.19	1.01	1.41

PODCS:postoperative delirium; NRS:numeric rating scale of pain; ICU:intensive care unit;
Combine procedures:combination of coronary artery bypasses and/or valve surgery and /or intervention of the ascending aorta;
OR:odds ratio; CI:confidence interval 95%.
Predisposing variables: Nagelkerke $R2 = 0.156$;
Precipitating variables: Nagelkerke $R2 = 0.214$
Combined predisposing and precipitating factors: Nagelkerke $R2 = 0.346$

Study II

Study II, the main finding was that out of 114 participants 26.3% developed dementia after cardiac surgery; at year one six participants (mean age 77.5), at three-years follow up nine (mean age 79.8) and at five-years follow up 15 participants (mean age 81.6). In the final multivariable logistic regression model a lower MMSE score before the operation and the occurrence of PODCS were factors independently associated with the development of dementia within a five years follow-up (Table 9 and 10).

Table 9. Participants' characteristics, regarding preoperative, operative and postoperative variables and univariate results included in Study II

Parameter	All Participants (*n* =114) Mean SD (%)	No Dementia (*n* =84) Mean SD (%)	Dementia (*n* =30) Mean SD (%)	Univariate *p* -value	
Preoperative variables					
Age (yr)	76.5 ± 4.4	75.9 ± 3.9	78.3 ± 5.1	0.01	a
Sex (female)	30.7	34.5	20.0	0.14	b
BMI	26.6 ± 3.9	26.7 ± 3.9	26.2 ± 3.8	0.56	
Impaired vision (glasses)	91.2	89.3	96.7	0.25	
Impaired hearing (hearing device)	23.7	22.6	26.7	0.65	
Living with partner	61.4	66.7	46.7	0.06	a
I-ADL dependent	34.2	31.0	43.3	0.22	
P-ADL dependent (yes)	3.5	1.2	10.0	0.06	a
Education (≥7 yr)	47.4	54.8	26.7	0.01	a
MMSE score (0-30)	27.0 ± 2.8	27.7 ± 1.9	25.1 ± 3.6	< 0.0001	a
MMSE score (<24)	7.9	1.2	26.7	0.0017	c
NRS pain (0-10) [1]	1.7 ± 2.0	1.7 ± 2.0	1.9 ± 2.2	0.60	
GDS score (0-15)	2.3 ± 2.0	2.3 ± 2.0	2.3 ± 2.1	0.91	
Depression	12.3	8.3	23.3	0.04	a
Sleeping disorder	30.7	34.5	20.0	0.14	
Diabetes	16.7	13.1	26.7	0.09	a
Cerebrovascular history	14.9	14.3	16.7	0.75	
Malignant disease	7.9	9.5	3.3	0.30	
Myocardial infarction (previous)	40.4	38.1	46.7	0.41	
NYHA I	3.5	3.6	3.3	0.92	
NYHA II	27.2	28.6	23.3	0.91	
NYHA III	57.9	56.0	63.3	0.87	
NYHA IV	11.4	11.9	10.0	0.94	
SAP mmHg	139.5 ± 21.2	139.1 ± 20.2	140.6 ± 24.2	0.74	
DAP mmHg	75.2 ± 10.3	75.1 ± 9.9	75.4 ± 11.5	0.87	
Numberd of drugs prescribed	5.7 ± 2.4	5.7 ± 2.2	5.6 ± 2.7	0.95	
Antikoagulans	87.7	90.5	80.0	0.14	
B-blockers	71.9	75.0	63.3	0.23	
Calcium channel blockers	28.1	27.4	30.0	0.56	
Antilipemic agents	69.3	76.2	50.0	0.01	a
Antidepressants	5.3	3.6	10.0	0.19	
Diuretics	36.8	31.0	53.3	0.03	a
RAAS -blockers	58.8	59.5	56.7	0.79	
Operative and postoperative variables					
CABG isolated	58.8	61.9	50.0	0.26	
Valve procedures isolated	20.2	16.7	30.0	0.12	
Combined procedure	21.1	21.4	20.0	0.87	
Operation time (h)	2.9 ± 0.9	3.0 ± 0.9	2.7 ± 0.8	0.11	
CPB time (h)	1.4 ± 0.6	1.4 ± 0.6	1.4 ± 0.6	0.97	
Ventilator time (h)	6.9 ± 3.3	6.5 ± 2.8	7.9 ± 4.4	0.06	a
ICU time (h)	22.3 ± 19.4	21.5 ± 21.8	24.6 ± 9.7	0.47	
PODCS	56.1	45.2	86.7	0.0004	a
Milrinone or Levosimendan required [2]	28.3	31.3	20.0	0.24	
Blod loss (l)	0.4 ± 0.4	0.5 ± 0.4	0.4 ± 0.2	0.77	
Volume load, blood excluded (l)	3.8 ± 1.1	3.8 ± 1.2	3.7 ± 0.9	0.52	

[a] Denotes variables tested in the multivariable models, with a P-value of <0,10.

[b] Denotes variables added at multivariable testing due to their expected principal importance rather than their statistical influence at univariate testing.

[c] Denotes variables (P-value <0,10) avoided in the multivariable models because of covariability aginst other used parameter.
BMI:body mass index; NRS:numeric rating scale of pain; I-ADL:instrumental-activities of daily living; P-ADL:personal-activities of daily living; MMSE:mini-mental state examination; GDS-15:geriatric depression scale; NYHA: New York Heart Association functional classification; SAP:systolic arterial blood pressure; DAP:diastolic blood pressure; PCI:percutaneous coronary intervention; CABG:coronary artery bypasses grafting; CPB:cardiopulmonary bypass; ICU: intensive care unit; PODCS: postoperative delirium; RASS:renin-angoitensin-aldosterone system;
combine procedure: combination of coronary artery bypasses and/or valve surgery and/or intervention of the ascending aorta;

[1] NRS pain: n= 113 one missing variable no dementia.

[2] Milrinone or Levosimendan required n=113 one variable missing variable no dementia.
p -values refer to univariate logistic regression analyses.

Table 10. Multivariable logistic regression analyses displaying factors independently associated with dementia, within five years after cardiac surgery in Study II.

Parameter	*p*-value	OR	Cl low	Cl high
Preoperative variables				
Age (year)	0.18	1.08	0.96	1.22
Sex (female)	0.02	0.19	0.05	0.76
MMSE score (0-30)	< 0.0004	0.70	0.57	0.85
Living with partner	0.04	0.30	0.09	0.93
Education (≥7 year)				
P-ADL (dependent)				
Depression				
Diabetes				
Antilipemic agents	0.03	0.31	0.11	0.90
Diuretics				
Operative and postoperative variables				
Age (year)	0.03	1.13	1.01	1.25
Sex (female)	0.23	0.52	0.17	1.53
PODCS	0.0039	5.75	1.75	18.89
Ventilator time ICU (h)				
Combined preoperative, operative and postoperative variables				
Age (year)	0.13	1.09	0.97	1.23
Sex (female)	0.13	0.38	0.11	1.33
MMSE score (0-30)	0.0005	0.68	0.54	0.84
PODCS	0.0016	7.57	2.15	26.65

MMSE:mini-mental state examination; P-ADL:personal activities of daily living;
ICU:intensive care unit; PODCS:postoperative delirium;
OR: odds ratio; CI: confidence interval 95%.
Preoperative variables: Nagelkerke R2 = 0.39, Overall %= 86;
Postoperative variables: Nagelkerke R2 = 0.28, Overall %= 73.7.
Combined preoperative, operative and postoperative variables: Nagelkerke R2 = 0.42 , Overall %= 79.82.

Participants who developed dementia had significantly lower MMSE scores on all six timepoints than those without dementia. The decline in MMSE scores from baseline to five years follow-up was larger in the group who developed dementia compared with those who did not ($p<0.001$) (Table 11).

Table 11. MMSE scores at each timepoint during the five years in participants with and without dementia in Study II.

Parameter	No dementia MMSE score	Dementia MMSE score	*p*-value
TP 1	27.7	25.0	< 0.001
TP 2	23.7	18.1	< 0.001
TP 3	25.8	20.8	< 0.001
TP 4	27.4	24.1	< 0.001
TP 5	27.5	21.7	< 0.001
TP 6	26.6	17.4	< 0.001

MMSE:mini-mental state examination;
TP:timepoint; TP 1: preoperative; TP 2: postoperative day 1;
TP 3: postoperative day 4; TP 4: 1 year after surgery ;
TP 5: 3 year after surgery; TP 6: 5 year after surgery

There were no differences in preoperative MMSE scores between those who developed PODCS and those without from baseline. However, MMSE scores differed significantly between the two groups (with PODCS and without PODCS) day one and day four postoperatively. Both groups had regained their preoperative MMSE scores at the one-year follow-up. MMSE scores differed significantly between those who developed PODCS and those without at follow-ups in year 3 and year 5 after surgery. Over the study period a decrease in mean MMSE scores was seen from baseline to five years follow-up, but the decrease was larger for participants with PODCS than for those without PODCS (p=0.001) (Table 12).

Table 12. MMSE scores at each timepoint during the five years in participants with and without PODCS in Study II

Parameter	No PODCS MMSE score	PODCS MMSE score	*p* -value
TP 1	27.4	26.6	0.136
TP 2	26.2	19.2	< 0.001
TP 3	26.7	22.9	< 0.001
TP 4	27.1	26.1	0.070
TP 5	27.2	25.2	0.009
TP 6	26.6	23.1	< 0.001

MMSE:mini-mental state examination; PODCS: postoperative delrirum;
TP:timepoint; TP 1: preoperative; TP 2: postoperative day 1;
TP 3: postoperative day 4; TP 4: 1 year after surgery ;
TP 5: 3 year after surgery; TP 6: 5 year after surgery

Study III

The analyses of the interviews in Study III revealed that the experiences of undergoing cardiac surgery affected participants afterwards. One year after cardiac surgery participant still described both painful and satisfying with memories of what happened around the time of the surgery that they were concerned about. Four themes were formulated: *Feeling drained of viability* with sub-themes having a body under attack, losing strength, and being close to death; *Feeling trapped in a weird world* with sub-themes having hallucinations, being in a nightmare and being remorseful; *Being met with disrespect* with sub themes feeling disappointed, being forced and feeling like cargo; Feeling *safe* with sub-themes being in supportive hands and feeling grateful.

The theme *feeling drained of viability* describes feelings of fragility and defencelessness in participants. The sudden onset of the illness was a distressful, exhausting and terrifying time. Their entire bodies were drained of strength after surgery. They described numerous physical sensations, e.g. loss of appetite, difficulties speaking or breathing. Participants also described how pain racked their body. Even with potent analgesics, the pain might not go away, leaving some participants disconnected from reality, with only fragmented memories of their hospital stay. Participants described how fragile life was before surgery, and when surgery turned out to be more complicated than expected, they realized they had been close to death.

The theme *feeling trapped in a weird world* involves descriptions of how participants suddenly felt dragged into a strange world of dreams. They experienced themselves as dreamy, woozy and confused. There were also some participants who felt they were completely clear and lucid although they were in a strange world. Participants described hallucinations as funny or, at worst, as a slightly odd experience. However, suddenly, ordinary things could change into something dangerous for no reason. Participants described it as being in a nightmare with feelings of frustration, pronounced fear, anger, anxiety and loneliness. They thought they were going insane. One year after some participants still described feelings of anxiety and worries over their weird experiences, as no one had explained PODCS to them. On the other hand, there were participants who did not experience anything weird during surgery. Participants also described how their own manner could change into something really unpleasant, bothersome and embarrassing. Sometimes they could not remember and they felt awful when relatives told them how they had been ashamed of their behaviour. Participants felt remorseful over their strange behaviour and talked about how they had to apologize and described these as difficult and shameful memories. These memories were still painful and seemed to bother them one year after surgery.

The theme *being met with disrespect* involves painful memories of what happened during their hospital stay, which made them question their confidence in the health professionals and healthcare. Participants described how they were not always looked after or given the care and treatment they expected. They were disappointed as this sometimes resulted in injuries and prolonged hospitalization. They described how they did not get appropriate information about complications or were not informed about the risk of developing PODCS. One participant told about a nurse being disrespectful when he asked questions and he felt that she ridiculed of him. Some participants described how they were forced to do things they said they could not manage e.g. forced to eat and forced to walk even if they did not have the strength. The hospital was described as unpleasant and disturbing, a suboptimal environment for rest and recovery. Participants described how they had been objectified and moved around like a piece of furniture into different rooms and new facilities. Some participants were transferred to their regional hospitals. Being exhausted and frail could mean that the journey was experienced as an unbearable ordeal.

The theme *feeling safe* involves experiences of deep gratitude towards healthcare professionals and positive experiences during the hospital stay. All participants mentioned that they felt safe and were well looked after. They expressed gratitude for being allowed to have cardiac surgery and for being given the chance of renewed life despite the unpleasant experiences. Feeling safe was expressed when professionals were competent and helpful and saw them as a person. Being in supportive hands was expressed when participants were convinced they would receive the best possible help and care. The preoperative information was described as important despite even though they did not find it easy to understand. Despite the information about possible complications they trusted the surgeon's decision. Next of kin, friends and fellow patients were described as a crucial support which made the hospital stay bearable. Some participants described cardiac surgery as a piece of cake, and that everything had gone smoothly. Even participants who found the surgery difficult were extremely grateful for the care they received despite all the concerns. They could now live for several more years and described it as a relief and a rediscovered freedom to survive cardiac surgery.

Study IV

In Study IV, the main findings were that a larger proportion of patients were diagnosed with PODCS based on the MMSE and OBS scale according DSM-IV-TR criteria compared to the Nu-DESC scale, both on day one and day four.

Table 13. Sensitivity and specificity of Nu-DESC comparisons to MMSE/ OBS (DSM-IV-TR) day one and day four in Study IV.

			Nu-DESC ≥ 2	
		n	Sensitivity (%)	Specificity (%)
Day I overall	True positive	42	65.6	
	True negative	74		94.9
	False positive	4		
	False negative	22		
Day IV overall	True positive	23	46.9	
	True negative	91		97.8
	False positive	2		
	False negative	26		

Nu-DESC:nursing delirium screening scale
Nu-DESC counts refer to true positive observations compare to MMSE and OBS
MMSE:mini-mental state examination; OBS:organic brain syndrome scale;
PODCS:postoperative delirium after cardiac surgery; Overall: all subtypes of PODCS
DSM-IV-TR:diagnostic and statistical manual of mental disorders 4th edition- text revision

Nu-DESC showed a low sensitivity and a high specificity compared with DSM-IV-TR criteria on both day one and day four (Table 13). The hypoactive symptoms were most common on both day one and day four according to MMSE and OBS scale (DSM-IV-TR). Nu-DESC did not detect all subtypes of PODCS. However, Nu-DESC identified the majority of patients with hyperactive and mixed symptoms whereas several with hypoactive symptoms were unrecognized (Table 14). Among those 78 who developed PODCS 29 were only delirious on day one, 35 both day one and four and 14 only on day four according to DSM-IV-TR criteria (Table 15).

Table 14.PODCS subgroups and comparisons between methods in Study IV.

	MMSE/OBS (n)	Nu-DESC (n)	Nu-DESC sensitivity (%)	Nu-DESC specificity(%)	*p*-value
Day 1 and/or Day 4	78	56	71.8	81.3	0.12
Day 1					
Overall	64	42	65.6	94.9	0.001
Only hyperactive	2	2	100.0	68.6	n.a.
Only hypoactive	40	28	70.0	82.4	n.a.
Mixed form	9	8	88.9	71.4	n.a.
Non-classifiable	13	4	30.8	67.4	n.a.
Day 4					
Overall	49	23	46.9	97.8	<0.001
Only hyperactive	3	1	33.3	82.7	n.a.
Only hypoactive	30	14	46.7	90.2	n.a.
Mixed form	7	6	85.7	85.9	n.a.
Non-classifiable	9	2	22.2	82.7	n.a.

MMSE:mini-mental state examination; OBS:organic brain syndrome scale;
DSM-IV-TR:diagnostic and statistical manual of mental disorders 4th edition- text revision
Nu-DESC:nursing delirium screening scale; n.a: not applicable
PODCS:postoperative delirium after cardiac surgery; Overall: all subtypes of PODCS
Nu-DESC counts refer to true positive observations.
P-value refers to McNemar comparison.

Table 15. Number of patients with PODCS according to MMSE/OBS (DSM-IV-TR) only day one, both day one and four and only day four in Study IV.

Parameter	MMSE/OBS n=	%
PODCS (only day I)	29/142	24.4
PODCS (both day I and IV)	35/142	24.6
PODCS (only day IV)	14/142	9.8

PODCS: postoperative delirium
DSM-IV-TR:diagnostic and statistical manual of mental disorders 4th edition- text revision
MMSE:mini-mental state examination; OBS:organic brain syndrome scale;

Discussion

The overall aim in this thesis was to investigate postoperative delirium in older people undergoing cardiac surgery with CPB; focusing on risk factors, dementia, patients' experiences and to evaluate a delirium screening assessment. The main findings in this thesis show that approximately 55% of patients developed PODCS. PODCS was independently associated with both predisposing risk factors; (diabetes, gastritis/peptic ulcer) and precipitating risk factors (volume load during operation, ventilator time in ICU, highest temperature and plasma sodium concentration while in the ICU). During the five years of follow-up after cardiac surgery 26% developed dementia. Both a preoperative reduced brain reserve capacity (preoperative lower MMSE scores) and PODCS were independent risk factors for the development of dementia. One year after surgery participants diagnosed with PODCS described painful memories of the staff and what happened around the time of surgery. The hospital stay could also be experienced as satisfying or safe. The participants were still concerned about these memories even one year after cardiac surgery. The most common symptom profile of delirium was the hypoactive. The Swedish version of Nu-DESC showed high sensitivity in detecting hyperactive symptoms but low sensitivity in detecting hypoactive symptoms of PODCS.

In this section I will first discuss the results in the four studies. The results from this thesis could indicate that patients who developed PODCS during cardiac surgery were actually suffering. In order to provide appropriate care there is a need to discuss procedures and routines and also to acquire a better understanding of what patients are going through in order to be able to avoid as well as relieve their suffering. Therefore, the results can be understood, and will finally be discussed, in the light of suffering as defined by Eriksson (187).

Incidence and symptom profiles

PODCS was common (55%) among older patients undergoing cardiac surgery with CPB (I, IV). The incidence of PODCS varies considerably between studies and has been reported as being from between 8-14% (188, 189) up to 46-67% (2, 41, 190). Studies reporting a high incidence, similar to that in Study I, used delirium assessments together with a cognitive assessment before and after surgery to meet DSM-IV-TR criteria for PODCS. However, the differences in incidence between studies may also reflect the different inclusion criteria regarding age.

PODCS was more common early after surgery on day one than day four, as in other studies (15, 190). The higher incidence may reflect the influences of anaesthetic exposure and pain relief during the first postoperative days (I, IV). However, PODCS was also common on day four postoperative (IV). Almost 30% of the patients were delirious on day four and 25% were diagnosed with PODCS on both day one and day four, and this is supported by results from previous studies (2, 15).

The most common psychomotor symptom was the hypoactive subtype of PODCS, with less obvious clinical manifestations of delirium (IV). Almost three out of four delirious patients on day one and day four developed the hypoactive subtype of PODCS, as shown in other studies (15, 54, 191). Hypoactive delirium also seems to be common among older medical inpatients (192) and among older people after femoral neck fracture surgery (16). A review investigating delirium in different populations shows that hypoactive delirium is associated with old age, dementia and degree of comorbidity (193).

Delirium that does not meet the DSM criteria, such as SSD, also seems to be common after cardiac surgery. Breu et al (2015) has reported a SSD incidence of 34% and a PODCS incidence of 12% (18). The study reported that only 2% of patients with SSD developed PODCS, and of those with PODCS 30% regressed to SSD. However, the outcome regarding mortality showed no difference (SSD vs PODCS) in patients with and without PODCS, apart from a lower rate of home discharge in the PODCS group. The significance of SSD seems not to be fully understood and the authors discuss the possibility that SSD might not represent an early state of manifest delirium (18). Skrobik et al (2012) reported that the implementation of a protocol for sedation and analgesia reduced SSD among critical ill patients. The implementation was associated with better outcomes, more patients remaining cognitively intact and reduced mortality over a period of 30 days (21).

To conclude, the incidence of PODCS is common both early and four days after surgery. To meet the DSM criteria for delirium it is important that delirium assessment, including a cognitive test, is used both before and after surgery. More research is needed to investigate the incidence of SSD and outcome among older patients undergoing cardiac surgery. It therefore seems feasible that when using Nu-DESC in clinical settings, PODCS should be discussed and interpreted as SSD, when some patients with 2 points or more may not meet the DSM criteria for delirium, in care as well as in research.

Predisposing and precipitating risk factors

To increase knowledge about the mechanism of the causative predisposing and precipitating risk factors of PODCS in older patients we used a multivariable logistic regression model. Study I shows that PODCS is multifactorial and when both predisposing and precipitating risk factors are combined the predicted strength of the model increases. Many risk factors have been confirmed in previous studies investigating predisposing and precipitation risk factors behind PODCS.

Study I shows independent risk factors for PODCS among older patients. The risk of developing PODCS increased 10% per year (I). It is well known that old age is a risk factor for delirium in different populations (45); this is also true in the period after cardiac surgery (50, 51). One study investigating PODCS shows that the incidence increased with age as follows; 22% (50-59 years), 42% (60-69 years), 75% (70-79 years) and 92% among 80-89 years old (194).

Preoperative diagnosis of diabetes increased the risk of PODCS 3.5 times (I), which is in line with results from other studies (189, 195, 196). However in a recently published systematic review the authors concluded that the evidence that diabetes is a risk factor for PODCS is inconclusive (51).

One strong risk factor associated with PODCS was a perioperative positive fluid balance (blood balance excluded) (I), which has not been reported previously. There are a variety of reasons for volume loading during surgery, hypotension being the most common. It is possible that volume loading is a surrogate marker for hypotension. It is also possible that increased blood pressure predicts PODCS (197) and blood pressure fluctuation predicts POD in non-cardiac surgery (198) and as such indicates changes in cerebral perfusion. However, haemodynamic complications after non-cardiac surgery were not associated with POD, but it was associated with greater blood loss during surgery, postoperative blood transfusion and a postoperative haematocrit below 30% (199). Due to lack of continuity the blood pressure registration was not sufficiently reliable to allow analysis of hypotension as an independent risk factor. Systemic inflammatory response is a well-known complication during cardiac surgery with CPB and increases the risk of PODCS (50). Such a systemic inflammatory response, mediated by a cascade of proinflammatory cytokines, including interleukin 8 (IL-8), leads to endothelial activation, extravasation of fluid and hypotension. It has been shown in animal models that the sepsis causes disruption of the blood-brain barrier and an enhanced cytokine transfer, ischemia and neuronal apoptosis (200). Levels of proinflammatory cytokine IL-8 have been associated with delirium in ICU and non-ICU patients (201). It is therefore reasonable to assume that the association between volume load and delirium may reflect the association between PODCS and systemic inflammatory response. Further indication of increased inflammation in the PODCS group was provided by a slightly increased postoperative body temperature (I). However, systemic inflammatory response (202) was not specifically investigated (I). Another reason for perioperative volume loading might be increased depth of anaesthesia, as general anaesthesia influences the sympathetic nervous system. Both volume loading and vasoactive pharmacological treatments are commonly accepted as treatments for hypotension caused by general anaesthesia. Reducing the depth of anaesthesia could thus possibly both reduce volume loading and exposure to anaesthetic medication. Studies have shown that when the brain function is monitored by using e.g. the bispectral index (BIS) to reduce anaesthetic exposure in older patients, the incidence of postoperative delirium was reduced after both cardiac surgery (203) and non- cardiac surgery (204, 205). However, Study I was not designed to elucidate the effects of anaesthesia exposure. Cerebral hypoxia during surgery has previously been described as a risk factor for cognitive decline and PODCS (206, 207), but we did not monitor cerebral hypoxia, as such monitoring was not used routinely during Study I. More research is needed to explain the role of positive fluid balance (blood balance excluded) as a risk factor.

Ventilator time in the ICU was also a risk factor for PODCS. The reasons for prolonged mechanical ventilation postoperatively are complex as it reflect both a complicated surgical recovery as well as use of anaesthetic, analgesic and sedative medications pre-, peri- and post-operatively. Local routines and procedures in clinical use during Study I allowed a wide divergence in the use of anaesthetic, analgesic and sedative medications. Studies have shown that the choice of anaesthetic medications used can reduce the incidence of PODCS (100, 101) and delirium in the ICU (208). However, a Swedish study reported that the interest in POD and POCD among nurse anaesthetists and anaesthesiologists seemed to be modest. Risk assessment, prevention and handling of POD and POCD seem to be less important than postoperative nausea and vomiting (PONV), pain, awareness or cardiovascular events (209).

Study I shows that increased plasma sodium concentration on day one was a risk factor for PODCS; this has been identified previously (210). However, in that study diagnostic criteria for PODCS was lacking as only severe psychosis due to delirium was reported as PODCS (210). In Study I, none of the patients were hypernatremic and there was no correlation with increased volume during cardiac surgery. Plasma sodium concentration in the ICU seems to be complex and may be a surrogate for unknown risk factors. The gastritis/ peptic ulcer variable also increased the risk of PODCS. This variable was borderline significant and should not have been included in the model. However, one possible interpretation may be that gastritis/peptic ulcer is a marker for physiological stressors before surgery and hence increases the risk of delirium (45).

Study I is based on a relatively small sample size in relation to the variables we analysed. Therefore, our findings should be validated in future studies concerning the same population. No risk factor analysis was conducted on the subgroups of PODCS as the hyperactive subgroup was so small. Therefore, further studies should investigate whether different risk factors can be identified in different subgroups of PODCS.

Delirium has been investigated over the last 5 decades (7, 22). Between 1964 and 2014 196 publications have been published resulting in the identification of 123 risk factors for PODCS (196). In a recently published systematic review the authors concluded that the evidence for risk factors associated with PODCS are; age, cerebrovascular disease, psychiatric condition, cognitive impairment, peri-operative blood product transfusion, mechanical ventilation time and postoperative atrial fibrillation (51).

There seems to be conflicting evidence among various studies concerning predisposing and precipitating factors as regarded risk factors for PODCS. Healthcare professionals need knowledge and guidance in order to be able to reduce PODCS among older patients. Whether an intervention to reduce the precipitating risk factors for PODCS can reduce the incidence of PODCS remains to be investigated. More research is needed.

Cognitive decline and dementia

Study I could show no difference in preoperative cognitive performance measured by MMSE scores between the groups with and without PODCS. One possible explanation for this finding might be that the included patients were a selected group of older patients (I). However, a reduced cognitive function preoperatively has been shown to increase the risk of PODCS (2, 25, 211), possibly indicating a reduced brain reserve capacity. One study shows that even a mild cognitive impairment and the patients' own subjective memory complaints seem to predict PODCS (42). Wu et al (2015) investigated the age-dependent relationship between preoperative MMSE score and POD among patients undergoing hip fracture surgery (212). A reduced preoperative MMSE score was associated with a higher incidence of POD. However, the optimal cut off score for MMSE was age-dependent. In patients aged≤80 years, the optimal cut-off score for MMSE was 18.4 points, and for patients aged > 80 years 21.4 points respectively. The study indicates that cut-off scores for MMSE differ for the development of POD, where patients below 80 years MMSE scores was lower than for those over 80 (212). Delirium is a multifaceted syndrome, but among younger and healthy patients delirium may occur only after many serious stimuli (45, 212). However, Study I indicates that cardiac surgery is demanding for older patients when both patients with and without reduced cognitive function preoperatively develop PODCS.

Study II shows that the initial drop in MMSE postoperatively was occurred in both groups but was greater in the PODCS group. Some participants in Study III described that they had only fragmented memories of cardiac surgery and felt out of control and had to ask what had happened. The reduced cognitive performance after surgery may explain why some participants' interviews were short and fragmented as all were delirious in Study III. Duppils et al (2007) asked patients undergoing hip surgery about their experiences of their delirium episode. Patients with MMSE scores below 25 did not remember the delirium episode (90). Similar findings have been shown in ICUs among delirious patients who had significantly less recall of their ICU stay than non-delirious patients (213, 214). However, memory loss can be expected as delirium includes changes in perception, orientation and memory thinking (9).

During a one-year follow-up (II) both those who were delirious and those who were not regained their preoperative MMSE scores, as they did in another study (2). A study among older people (≥ 65 years) with and without surgery shows that the MMSE score tended to decline after a prolonged hospital stay (> five days) (215). More than 50% of the patients exhibited cognitive decline at six months after hospital stay. However, for patients who had undergone surgery MMSE returned to its preoperative score. The authors discussed the possibility that the decline in MMSE score may reflect patients who developed delirium after surgery which they later recovered from (215).

There are studies which use a more extended battery of neurocognitive tests to investigate cognitive decline in patients undergoing cardiac surgery. Selnes et al (2008) investigated a group of patients with coronary artery disease (216). They showed that a mild cognitive decline was observed in both those who undergone CABG surgery (mean age 71.9) and those who did not (mean age 70.9). No significant difference was seen between the groups during the six-year follow-up. The cognitive decline seems not to be specific to the cardiac surgery after six years. However, the study was nonrandomized (216). Another study investigating neurocognitive function after CABG surgery over a five-year follow-up shows that cognitive decline at discharge was a predictor for reduced cognitive function in the long term (217). Since neither of those two studies (216, 217) reported the occurrence of PODCS and the inclusion criteria differ the results are difficult to interpret. However, a cognitive decline immediately after surgery seems to increase the risk of reduced cognitive function years after surgery.

Study II shows that a lower score of MMSE preoperatively and the occurrence of PODCS were factors associated with development of dementia during the five years of follow-up. Among participants who developed dementia 7.9% showed a reduced MMSE score of below 24, indicating a reduced brain reserve capacity before surgery. During the five years of follow-up the drop in the MMSE score was greater both in the group with PODCS (3.5 points) and among those with dementia (7.6 points). A study in community-dwelling including elderly people (mean age 76) shows that during a five-year period MMSE scores changed more than two points among 48% of the elderly people (218). Among participants in Study II the drop in MMSE seems to be greater during the five-year period among those who developed PODCS and dementia. One explanation might be that participants in study II might be sicker since they all had CVD and multiple diseases.

To our knowledge Study II is the first longitudinal cohort study focusing on PODCS and the development of dementia after cardiac surgery. In total 26% of participants developed dementia during a five-year follow-up period. The prevalence of dementia differs between ages and countries (219, 220). One review showed that age-specific prevalence of dementia in European populations almost doubles every five years. The prevalence was as follows: in the age group 60-65 years (0.15%); 65-70 (1.2%); 70-75 (3.6%); 75-80 (7.6%); 80-85 (21.3%); 85-90 (31.6%); 90-95 (31.6%) and above 95 (44.7%). However, most of the studies were carried out in southern Europe (219). A population-based study performed in northern Sweden among the very old reported a prevalence (2005-2007) of dementia at age 85 (28.2%), 90 (39.8%) and 95 and older (45%) (149). Between the periods 2000-2002 and 2005-2007 the prevalence in the total sample increased from 26.5% to 37.2%. During the study period there was an increased proportion of participants who had undergone cardiac surgery and an increase in treatment with medications for cardiovascular disease and dementia symptoms (149). It is difficult to compare the prevalence of dementia among studies as there are variations in methodology but it seems to be higher in Study II than in other studies.

Study II showed that older patients who developed PODCS increased the risk for dementia almost 8-fold. The great majority (87%) of those who developed dementia had been delirious after surgery. A lower MMSE score and PODCS might be a marker of a vulnerable brain in older patients. Older patients undergoing cardiac surgery are at great risk of developing PODCS. Inouye et al (2014) emphasize that brain pathophysiology of delirium serves both as a marker of brain vulnerability with reduced reserve capacity as well as a potential trigger for permanent cognitive impairment (45). It has been shown among older people in various populations that delirium is a risk factor for dementia (161, 162). It is worth noting that, in a selected group of older people without documented dementia on admission, more than a quarter developed dementia during the five-year follow-up (II). In a review that investigated the link between cardiac diseases and dementia it was reported that heart diseases and cardiovascular risk factors, manifested in midlife, seem to be associated with dementia. Early prevention and treatment may reduce the onset of dementia but more research is needed to establish this (221). It remains to be investigated whether the prevention of PODCS can reduce the risk of later development of dementia among patients with CVD.

Delirium assessments

Study IV shows that Nu-DESC used in clinical care by nurses has low sensitivity. Nu-DESC failed to recognize PODCS in one third of the patients on day one and almost half on day four according to DSM-IV-TR. Nu-DESC did not recognize the hypoactive subtype of PODCS (IV). In other studies NU-DESC has been shown to have a high sensitivity and specificity when used (sensitivity/specificity): in hemato- oncology internal medicine inpatients (86%/87%) (78); in ICUs (83%/81%) (64); recovery rooms (95%/87%) (39) and on surgical wards (98%/92%) (80). One possible explanation may be that in the previous studies that validated Nu-DESC it seems to have been carried out by trained staff or trained researchers. Another study in an ICU shows that Nu-DESC had 100% sensitivity and 86%specificity (222). However, in that study Nu-DESC was based on the clinical diagnosis of delirium, in turn based on ICDSC, and was not evaluated according to DSM IV criteria for delirium

In Study IV, Nu-DESC's low detection rate may also reflect daily practice in CSD in contrast to previous studies (64, 78, 80). The difference might be that Nu-DESC assessments were gathered from CSD at three different levels of care (ICU, step-down unit, general ward). The CSD is designed to secure a high level of care and relocation between different levels of care. This means that nurses only have responsibilities for patients during a limited period which might make it difficult for them to know if the patients' cognition differs from their preoperative level. The staff ratio differed between the three care levels in CSD and may also explain the lower sensitivity on day four (general ward) when the staff ratio was lowest (IV). Preoperative screening for cognitive function affects the nurses' opportunity to draw attention to patients' cognitive changes during their hospital stay. It is not always possible in emergency or acute situations to perform a preoperative cognitive test. In such cases a history from the next of kin can be important in establishing the patient's baseline performance (45, 223). The month's backwards test (MBT) (224, 225), a bedside test, seems easy to use (20 seconds) and efficient for testing attention and cognition. One study shows that when the item "What is the day of the week?" combined with the item "Month's backwards?" was used to identify delirium the sensitivity was 93% and specificity 64% (226).

Another explanation for the low sensitivity of Nu-DESC in detecting it is that PODCS also presents different psychiatric symptoms such as emotional, psychotic, mixed, emotional and psychotic and non-classifiable psychiatric symptoms (73). Depression is also common before and after cardiac surgery (133-135); in Study IV 14.8% of the participants were diagnosed with depression before surgery.

However, other assessments used for delirium detection have also proved inadequate when they have been used in clinical care. Neufeld et al (2013) show that both Nu-DESC and CAM-ICU in a Post-Anaesthesia Care Unit (PACU), have low sensitivity, 32% and 28% respectively, and a high specificity >90% (40). Eijke et al (2011), in an evaluation of daily practice of CAM-ICU used by nurses in ten ICU centres, showed a sensitivity of 47% and specificity of 98%. In only 30% of the ten ICU centres were delirium assessments used as a part of the standard evaluation by an intensivist. The authors discussed the possibility that the bedside nurses may lack motivation to perform the CAM-ICU when it is not used as a standard procedure to evaluate the results in the treatment of their patients (227). In Study IV, the Nu-DESC score was not evaluated and used in the treatment of patients during their hospital stay. Further, only patients included in the study were screened for PODCS using Nu-DESC. It is therefore possible that the nurses in CSD perceived that the primary purpose of using the Nu-DESC was only for research and this is supported in another study (228). The nursing staff on the CSDs three sections participated in only a one-hour introductory session. A study investigating an education intervention showed that, with a combined didactic and scenario-based education, the ability of ICU staff to recognize delirium using ICDSC was improved (70). A more extensive education programme and hands-on training may have increased the Nu-DESC sensitivity (IV).

A recent published review investigated psychometric properties and feasibility of assessments for the detection of delirium in older hospitalized patients. The study included 28 assessments, and the authors concluded that CAM and Nu-DESC appeared to be the most adequate assessments (229). According to this thesis it seems to be important to screen for delirium and using an assessment to detect delirium improves the detection considerably. It is plausible that it is not of significance which delirium assessment you use but rather that you do use one. A common language used in assessments for delirium may ensure a response to this critical syndrome and seems to support care delivery (230). Therefore assessments for delirium must be implemented in the CSD as a standard procedure to improve the care and avoid unnecessary suffering. More research is needed to investigate whether Nu-DESC used in clinical care in combination with a cognitive test increases the sensitivity for PODCS.

Experiences of cardiac surgery

Study III aimed to illuminate patients' experiences of undergoing cardiac surgery. Even one year after cardiac surgery memories of what happened still caused participants concerns. Being old and undergoing cardiac surgery was a multifaceted, complex and distressful experience for participants who all had been delirious.

The theme *Feeling drained of viability* was concerned with how recovery after surgery was unpleasant and demanding for participants and meant struggling with their bodies which were affected by the surgical procedure. Participants expressed that they did not take the future for granted. It has also been reported elsewhere (99, 231, 232) that cardiac surgery is challenging and demanding when it involves a risk of dying as well as a hope for life. Participants' experiences were complex and they lost control of their bodily functions. Other studies have reported that cardiac surgery can be interpreted as suffering weakness, due to disturbed body function (231, 233).

It is important to address the fact that one year after surgery the participants' experiences of being in a weird world affected them in the form of painful memories (III). Another study showed that patients with and without delirium in the ICU remembered factual events up to two years after discharge (213). However, patients diagnosed with delirium had poorer recall than those without. Ringdal et al (2010) investigated the long-term perspective of health-related quality of life among trauma patients (234).

Patients with memories of delusions experienced poorer health-related quality of life and more of them suffered depression and anxiety compared to those without such memories (234). It seems plausible that participants in Study III could have been exposed to the same risks. More research is needed as optimal recovery after surgery is important. Older patients should not have to waste their energy on unpleasant experiences such as nightmares or being exposed to the risk of developing PODCS.

All participants in Study III were diagnosed with PODCS. It should be noted that some participants were convinced that they had not been delirious even if they described experiences of delusions and nightmares. It is possible that participants did not understand the concept of delirium, or did not want to share their memories for some reason, or did not actually remember.

Patients were afraid that someone would make a mistake (231, 235), and they experienced lack of care or lack of information which meant that they did not understand what was going on during and after cardiac surgery (236). The participants in Study III shared similar experiences and were, according to our interpretation, met with disrespect. The poorly designed and organized environment seemed to make participants feel uncomfortable and exhausted, which contributed to the feeling of being like a cargo. Studies have shown that the design of hospital rooms seems to influence the incidence of delirium (106, 107).

However, despite difficulties and unpleasant experiences during their hospital stay all the participants described feeling safe and looked after. The support from next of kin, fellow patients and healthcare professionals was important and made them feel safe. Similar findings, regarding these factors which are essential to the restorative process and the return to normalcy after CABG surgery have been reported in another study (231). Among patients who have been cared for in an ICU memories seemed to fade or disappear over a one- and three-month follow-up (237). During follow-up at three months participants who remembered their stay in ICU mostly recollected memories about their next of kin and the recollections even increased between the follow-ups (day three 69%, at one month 79% and at three months 81%) (237). It seems that next of kin are of great significance to patients in serious conditions. Another question to be raised concerns the significance of talking about and telling someone about your memories of the hospital stay. Further research in this field is needed.

The participants were grateful to healthcare professionals when they were competent and saw the participants as persons (III). Nurses who offer ‘the little extra’ and are willing to go beyond their obligations may confirm patients and see them as fellow human beings (238, 239). Being present and listening to the patients' experiences seems to reduce suffering (96, 98, 240).

Samuelsson (2011) showed that most patients have both unpleasant memories, such as life-threatening experiences, frightening unrealities, and distortions as well as pleasant memories such as good caring and support during their ICU stay. The author concluded that despite the unpleasant memories predominating their impact seemed to be balanced by the pleasant memories (241). Similar results have been shown among patients in acute care hospital (235) and psychiatric wards (242). Having trusting interactions with the staff make up for the confusing care and poor environment (242). It seems plausible that participants' memories would have faded or blurred one year after surgery but their memories of good or bad care, pleasant or unpleasant memories, seemed to persist even that long after cardiac surgery (III).

Nurses are very important in providing good care for older people undergoing cardiac surgery. They are the primary care givers and hence crucial for the patients' wellbeing. Nurses are close to the patient and need to listen and confirm patients' needs to make them feel safe during surgery (III). It is also important that nurses consider the next of kin as potential resources for patient recovery after surgery. Being confirmed is important for feeling safe during a hospital stay.

Interpretations of the findings

Florence Nightingale already highlighted suffering when she closely observed that the environment and care actually increased patients' suffering. She observed that patients needed more specific care after surgery and described how the rooms had to be arranged to enable closer and more extensive observations of patients (243). Eriksson (1992) stated that alleviation of suffering has always been the most important in care, and therefore suffering is the key motif for all caring (244). Eriksson (1997) claimed that in order to understand the patient's world, a caring perspective must be applied, and the individual suffering of each person must be understood (245). To alleviate patient suffering it is important to understand that the suffering looks different from patients' and healthcare professionals' perspectives (246).

According to Eriksson (1992) health and suffering belong together and are natural parts of life (244). Suffering is a personal experience that can have many faces and forms, and can be visible or invisible to others. Illness can lead to suffering but suffering can be experienced beyond illness. According to Eriksson, patients can experience three forms of suffering; suffering from illness, suffering from care and suffering from life. Suffering from illness includes experiences of illness, such as bodily pain emanating from a specific organ or body part. However, the pain is not just physical but also affects the person as a whole. Suffering from illness can be caused by treatments and all the unexpected circumstances related to the illness. For example patients may feel ashamed of not taking care of themselves as they should, of not following advice or of being dependent on care (cf 187 p 83-84). Suffering from care includes experiences related to the care situation. Eriksson claims that the most common suffering from care occurs when one's human dignity is offended, but condemnation, punishment and lack of care are also serious forms of suffering (cf 187 p 87). Suffering from care can result from the ignorance of the staff and their lack of knowledge and skill. Hence, a patient's suffering might not be caused by a deliberate action (cf 187 p 98). Finally, suffering from life includes life itself, what it can bring in terms of e.g. "broken love or facing death" (cf 187 p 83). It seems that all forms of suffering can be intertwined (187, 247). It is therefore important to understand suffering and in healthcare to recognize those patients who suffer (244).

All the studies in this thesis can be interpreted according to the concept of suffering from illness due to predisposing and precipitating factors and to an even greater degree for those who developed PODCS. It is reasonable to assume that older patients with multiple diseases are fragile, more vulnerable to complications and at risk of suffering from illness (II, III). All the participants in this thesis seem to have been at risk of suffering even before surgery as their CVD made them ill. Some also had diseases such as diabetes, gastritis /peptic ulcers, depression and some were in pain (I, II, IV). Even in the interviews one year after surgery participants described experiences that could be interpreted as suffering from illness due to their CVD (cf 187 p 82). They described how vulnerable they were, and how their lives were fragile (III).

The precipitating factors for developing PODCS seem to encompass all mandatory procedures related to cardiac surgery such as volume load during operation and increased ventilator time in the ICU (I). Since these factors might increase the risk of developing PODCS this situation could be interpreted as suffering from illness for these patients (I). The combination of all risk factors increases the risk for PODCS especially for fragile older people. In Study III participants described experiences from their hospital stay and the challenges related to it and to their recovery. *Feeling drained of viability* and *Feeling trapped in a weird world*, indicate suffering from illness (cf 187 p 83). This interpretation is supported by other studies (91, 95). One study reported that confusion among older people admitted to hospital was a frightening experience (95). Delirious, critically ill patients talked of a state of chaos resulting in feelings of vulnerability and fear (91). In Study III some participants remembered only fragmented episodes of what had happened during their hospital stay. Whether or not the patient remembers, delirium episodes seem to be distressing experiences (248) and might also point to suffering from illness (III).

Dementia has a great impact on a person's life. It entails a progression of cognitive losses that the person must adapt and adjust to. A review by de Boer et al (2007) shows that dementia is not only about memory losses but also about the gradual loss of the skills needed to execute normal activities. When people who develop dementia realize that something is wrong, it might give rise to feelings of insecurity, confusion, fear, anger, sorrow and anxiety (249). One plausible interpretation is, therefore, that some at least of the participants in Study II experienced suffering from illness due to dementia.

One year after surgery participants still had painful memories of the staff and what had happened during their hospital stay (III). It seems that the routines related to the procedures in cardiac surgery and the care provided may not be optimal for older patients. It appears possible that patients experienced suffering from care when PODCS was not detected (IV). The results of Study IV indicate that the nurses lacked both knowledge and skills, and perhaps did not have sufficient and reliable assessments from which to identify hypoactive PODCS. It is important that nurses are made aware that patients with less obvious symptoms of delirium, such as hypoactive symptoms, could still have PODCS (IV). One explanation for the failure to recognize PODCS might be that nurses assessed hypoactive symptoms of PODCS as tiredness after surgery and as 'they need` to rest (IV). It also seems reasonable to assume that as nurses were focused on monitoring patients and vital signs and lacked knowledge, they did not recognize the symptoms of delirium, such as cognitive decline (II, IV). Similar results have been shown in a study investigating nurses' recognition of delirium in the ICU (250). This study reported that older patients with heart failure treated pharmacologically with benzodiazepines could be at risk of under recognition of delirium, as their medical condition and the medical treatment as such constitute a barrier to recognition. Hence, nurses might miss the delirium (250). In Study III we conclude that there may be a possibility that nurses deliberately avoided asking patients about delirium to spare them further distress or under the assumption that they would not remember. If that was the case it indicates that these nurses may have intended to avoid causing the patients further suffering but their lack of knowledge might actually increase the patients' suffering from care (cf 187 p 98).

As patients were not preoperatively assessed for cognitive decline in clinical care the risk of PODCS as well as dementia were not assessed. Thus, no preventive strategies were easily available and these vulnerable patients were not recognized (II). As their needs were not seen or taken care of, neither before nor after surgery, this could lead to suffering from care (cf 187 p 92).

If nurses fail to recognize reduced cognitive performance in patients, they might not be aware of their reduced ability to understand or follow instructions before and after surgery. That is what might have happened to one of the patients in Study III who regretted not following the treatment recommendations, which led to additional surgery. Also some participants described how pain racked their body and did not go away despite analgesics (III). It may be possible that nurses did not even recognize patients in severe pain.

Patients in Study III also described how nurses did not take their experiences seriously and how they felt deceived by the healthcare. Not every nurse seemed to understand what patients were going through. Not being seen is a way of being humiliated (cf 187 p 92-93) (III, IV). Patients felt that they could not confide in the nurses, or ask the questions they wanted to ask, or that they did not receive enough information (III). Not knowing what happens and why is a form of suffering from care (251). No care or lack of care seems to be common occurrences within healthcare (95, 252-254).

The theme *Being met with disrespect* indicates that in some way care in CSD is characterized as a production line, especially since participants described how they had to change rooms and move around constantly to new facilities during their hospital stay. It is reasonable to assume that patients experienced the hospital environment as poor and disturbing; this can be interpreted as suffering from care. The themes *Feeling drained of viability and Feeling safe* indicate that participants could be suffering from life itself when before surgery they could not take the future for granted and after surgery realized that they could live for several more years (cf 187 p 83).

Ethical reflections

There were some ethical considerations to take into account when studying older patients and people in various vulnerable states. The participants included in this thesis were sick due to their CVD even before the surgery. During the follow-ups I became aware that some participants were even more vulnerable. They had become both physically weak and developed additional diseases such as cancer stroke with aphasia, dementia, depression and more severe hearing problems. It was, therefore, even more important that the research proceeded respectfully and that their needs were taken into account during data collections.

For each assessment during the hospital stay and home visits participants were again informed of the purpose of the study. The intention during the interviews was to be sensitive to participants needs. Patients were offered the chance to answer the questions in a single room during the hospital stay. They were also offered the possibility to contact the interviewers after the home visits if they had any concerns or further questions.

The role of a researcher in a healthcare environment is complex. The author and research RN could be perceived as a friend but also as a nurse. Notably, during their hospital stay and some home visits, participants may have seen the author and the research RN as nurses instead of researchers. This was ethically reflected on in the research group during the data collection (255).

The data collections, including all assessments, were extensive and the whole interview could have made participants tired or even exhausted. The nature of some questions could also be considered intrusive. However, the author and research RN were observant of their reactions and if the participant showed any signs of inability to continue the interview sessions were ended (186). During the follow-ups the hearing ability of some participants deteriorated. The questions were read out loud, and if participant's had a more severe hearing problem they had the opportunity to read the questions for themselves. Giving support in completing a questionnaire is valuable for obtaining valid data from very old people (256). However, my experience was that participants generally seemed to find the interviews a positive experience and often continued the social interaction for a while after the interviews were completed. They wanted to help someone else. Their eagerness to continue and not withdraw from the study could be interpreted as their being positive. There are studies which report advantages from being given the opportunity to tell a self-story that can help one to understand what had happened. In this light it might be possible that those participants who agreed to continue with the studies included in this thesis appreciated the opportunity and participated for that reason (257, 258).

Methodological considerations

This thesis applied a combination of both qualitative and quantitative methods in order to gain a broader insight regarding the PODCS (259). The studies included in this thesis have both strengths and limitations that must be considered.

The strengths of the studies (I-IV) include their being based on comprehensive assessments, including cognitive testing both before and repeatedly after surgery and during five years of follow-ups. All interviews were face-to-face during the hospital stay and almost all at the follow-ups. Only two researchers (author and one research RN) collected data for all the studies (I-IV). The intention was for the same researcher to meet the same participant at all the follow-ups, but this proved impossible on all occasions. Another strength is that the participants were followed up over a five-year period. The number of participants lost in the follow-ups can be considered rather small considering the huge geographical area - half of Sweden – covered by the studies.

The cohort study in this thesis is designed in line with Study IV, which was the first study sample collected. The results may therefore be limited because of the relatively small sample size in relation to the large number of variables systematically extracted for analysis in Studies I and II.

In Studies I and IV, the preparation and special training in carrying out delirium assessments, as well as other assessment scales, could have been more extensive. A test-retest between the two nurses to reach consistency in their assessments could have been performed in a more systematic or extensive way.

The MMSE scale was the only assessment used for cognitive performance in the cohort (I-IV). A more extended battery of cognitive tests would have been desirable (260, 261). It is known that the MMSE seems to be less sensitive to debut mild cognitive impairment but highly to moderately sensitive to moderate to severe cognitive impairment (168). The MMSE is often used to investigate changes in cognitive performance in research and in clinical care (2, 168, 260). However, the assessment can be influenced by education and age (261). In Studies I and IV there were no differences between participants with and without PODCS regarding education level. On the other hand in Study II there was a difference between participants with and without dementia. The role of training also has an effect on performance in MMSE and must be taken into consideration, especially during the hospital stay when the MMSE was repeated within a short time (I, II, IV) (168, 262). During their hospital stay participants were examined for PODCS only on days one and four after surgery, it is therefore possible that some delirious patients were not recognized. Other factors during the hospital stay that we were unable to explore further were pharmacological interactions (use of anaesthetic, analgesic and sedative medications and medications for treatment of PODCS) which may have affected cognitive performance. Further, five participants were offered a structured interview by telephone and the MMSE scores were recalculated according to Roccoforte (169). Use of a another telephone assessment such as the 26-point Telephone Version of the Mini-Mental State Examination might have been more appropriate (II) (263). However, none of these participants showed any symptoms that could indicate dementia.

The diagnosis for delirium, dementia and depression were based on the Diagnostic and Statistical Manual of mental disorders (DSM-IV-TR criteria). The DSM is a guideline for improving and establishing diagnosis of various mental disorders in clinical care, published by the American Psychiatric Association (10). However, the diagnosis of delirium can also be established using assessment scales for delirium (ICDSC, Nu-DESC) (75, 78) and depression can be established using assessments scales developed to assess depressive symptoms (GDS-15) (175). Those scales, ICDSC, Nu-DESC or GDS-15, have a cut-off score indicating a clinical diagnosis of delirium or of depression respectively. There are also assessments scales (CAM) using an algorithm on four features of delirium based on DSM-III criteria (71). Delirium, depression and dementia can be difficult to distinguish from each other when the diagnoses have a similar symptomatology and seem to overlap among the very old (264).

Dementia is a general term in DSM-IV-TR and includes many specific diseases that reduce the brain capacity. Therefore MMSE score was not used as the sole criterion for dementia diagnosis; further medical or neuro psychological examination was necessary (168). In Studies I, II and IV we used a more extensive assessment scale (OBS scale). The OBS scale assesses clinical manifestations of various psychiatric symptoms (66, 170). In combination with the MMSE (167, 265) it may increase the possibility of detecting different organic brain disorders. Unfortunately no specific dementia diseases could be diagnosed in Study II. The diagnosis for dementia and depression was set when the longitudinal cohort study was completed (2014). It was based on the decision of one physician, experienced in geriatric medicine, who evaluated all collected assessments and interviews

(MMSE, OBS-scale, GDS-15, Katz-ADL, medications). The diagnosis of dementia was not set after having access to medical records during follow-ups and no brain images/x-rays or more extensive examinations were performed; this must be considered a limitation. An experienced psychiatrist may also be needed to ascertain a clinical diagnosis of depression. On the other hand it was possible to obtain important and necessary information from the assessments and interviews and from healthcare professionals and next of kin.

The diagnosis of PODCS was set after the data collection in 2009 by two experienced researchers (one RN, one physician) specialized in geriatric medicine. To establish a PODCS diagnosis directly at the bedside, based on more than one experienced researcher, may improve the diagnosis. However, the diagnosis of delirium was based on several steps; first independently but then consensus was established by those two. This was based on the DSM-IV-TR criteria for delirium.

Nu-DESC was based on observations during the shifts and the author and the research RN only assessed the patients on two occasions postoperatively (day one and day four). The evaluations of the nursing staff in CSD were not performed at exactly the same time and this may have affected the NU-DESC sensitivity. The nursing staff at the CSD's three sections participated in an introductory session lasting only one hour. Approximately 50% were given an introductory information session. However, the nurses had a two-week run-in period for Nu-DESC before the study started (I, IV). A more extensive education programme and hands-on training could have increased Nu-DESC sensitivity.

Studies I and II was based on a relatively small sample size in relation to the high number of variables analysed. Other contributing factors behind PODCS are to be sought among a variety of factors beyond those tested (I). The influences of blood pressure and CPB during surgery were not investigated; crystalloid and colloid infusions in the ICU were not monitored. Other contributing factors behind dementia also have to be taken into account when interpreting our results (II). This can be embolic mechanisms during surgery and other injuries to the brain, such as cerebrovascular accidents early and late after surgery (266). Therefore, the findings should be validated in future studies in older patients undergoing cardiac surgery.

In the longitudinal cohort (II) it may be possible that participants who dropped out, died or declined to participate may have had dementia and this might have led to an underestimation of dementia. A larger cohort would also have been desirable and no control group with CVD who had not undergone cardiac surgery was recruited for comparison in Study II.

Study III was qualitative in design. The methodological considerations will be discussed in terms of trustworthiness i.e. credibility, dependency and transferability (184, 259). Credibility was addressed already in the planning stages of the study. Participants with and without PODCS were interviewed but only the interviews with those who had been delirious were analysed for Study III. The author and RN did not know whether the participants had been diagnosed with PODCS when they performed this interviews. The semi-structured interviews were designed to allow qualitative content analysis (183, 259). The author and research RN were not experienced interviewers, which may be reflected in the quality of the interviews. This could be seen as a limitation. However, both interviewers and participants had already met in the hospital, which seemed to create a trust in the interview situation as participants willingly shared their experiences. Some interviews were rich and some, while fragmented, still provided a wide range of experiences in connection with undergoing cardiac surgery. The analysis process of the transcribed text followed the suggestions of Graneheim and Lundman eg (184). Credibility can be discussed in relation to the analysis process. The first interviews were analysed and discussed among the author and researchers experienced in qualitative methods in order to achieve consensus in the interpretations. The researchers also returned to the original text in order not to lose the meaning when codes, sub-themes and themes were formulated. Quotations from the text were used when presenting the findings to allow the reader to assess the plausibility of the interpretations (184).

To achieve dependability the interviews were semi-structured (184). The same areas were covered in all interviews and the same main questions were asked. Lindseth and Norberg (2004) argue that it is difficult to be free from a pre-understanding (267). The authors' and the research RNs' pre-understandings were discussed within the research group to clarify their significance in the analysis process. Both the author and the research RN worked at the CSD and were familiar with the research context. According to Krippendorff there is always a degree of interpretation when approaching a text as there is never one single meaning (183 p 22).

Therefore, there may be several interpretations of the findings. In order to achieve dependability all authors in Study III were involved and the interpretations were regularly discussed during the analysis process. An independent research group, experienced in the method, also evaluated the reasonableness of the results. Finally, transferability was addressed when the findings were reflected on in relation to relevant literature. It seems reasonable to believe that the conclusions from Study III may be transferable to other contexts where older people are exposed to complicated treatments or surgeries. However, such transferability to other contexts must be decided by the reader (184).

Conclusions

Delirium was common among older patients and both predisposing and precipitating factors contributed to postoperative delirium. It is possible to affect some of them, however; future randomized studies must be conducted. It seems that patients should be screened for cognitive function preoperatively and also assessed for PODCS. These patients should be followed up to enable early detection of symptoms of dementia. Whether prevention of PODCS may reduce the risk of future dementia or not remains to be studied. To reduce unnecessary suffering for patients as well as next of kin is an important duty for health care professionals. Both patients and next of kin should be informed preoperatively about the risk for PODCS and also offered follow-up contacts after discharge. Nurses need to support and recognise these patients, e.g. being present, listening to patients' experiences and asking questions about unfamiliar experiences. The Swedish version of Nu-DESC should be combined with cognitive testing to better detect hypoactive delirium, but further research is needed. To summarize, health care professionals need more knowledge on postoperative delirium in order to prevent, detect and treat delirium to avoid and relieve the suffering the syndrome might cause.

Clinical implications

In order to provide good and appropriate care, and to alleviate and prevent unnecessary suffering in older patients undergoing cardiac surgery, changes need to be implemented. Both patients and next of kin must be informed of and prepared for the risk of developing PODCS. The information must be designed for older patient's needs for information, support and care. In addition, the information provided must be followed-up by nurses in order to ensure that it has been understood. Next of kin should be invited to be present as support for patients during their hospital stay.

An interdisciplinary delirium team, working closely together, seems to be necessary in CSD. Preventive strategies need to be implemented to enhance the care. The healthcare environment and routines should be adapted to meet older patients' needs. The preventive strategies and new routines should be based on knowledge of predisposing and precipitating risk factors from high quality studies.

Older patients should be screened for cognitive function before surgery and for PODCS to increase the ability to prevent the syndrome. An assessment for delirium combined with a cognitive test should be used as a standard procedure for the detection of PODCS. After cardiac surgery patients should be followed-up, so they can be provided the help they need and also get help in understanding what happened, and if necessary. Healthcare professionals who are responsible for these patients after their hospital stay should also be offered education about delirium. Patients' psychiatric symptoms and cognitive abilities, early and late after surgery, need to be followed-up. Those with reduced preoperative brain reserve capacity and those who develop PODCS should be followed up after discharge to enable early detection of dementia symptoms and implementation of preventive interventions. Hopefully, by doing this, it will be possible to reduce unnecessary suffering in older people after cardiac surgery.

Future research

During my PhD period new questions arose. Research is needed to investigate how preoperative and postoperative information influences older patients' experiences of PODCS and their hospital stay. There is a lack of studies investigating patients' experiences of using antipsychotic medication when they are delirious after cardiac surgery. More research is also needed on CPB and how the use of anaesthetic medication influences PODCS and dementia. Further, research is needed to evaluate the impact that PODCS has on patient safety, depression, quality of life and economical aspects on healthcare. Randomized controlled trials are needed to investigate whether multifactorial interventions can reduce PODCS. Longitudinal studies after PODCS are lacking and the question of whether prevention of PODCS can reduce the risk of cognitive decline and future dementia after cardiac surgery remains unanswered. We also need to explore how Nu-DESC is used by healthcare professionals' in clinical care and its ward-related consequences for the patients. Research is also needed to establish whether Nu-DESC combined with cognitive testing increases nurses' detection of PODCS.

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"You can check-out any time you like, but you can never leave!"

Lyrics, Eagles. Hotel California, 1976.

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Bilagor

Svenska versionen av Nu-DESC (The Nursing Delirium Screening Scale)

1. I slutet av varje arbetspass, dokumentera förekomst eller frånvaro av de fem olika symtomen på delirium.
2. Använd följande definitioner:
   a) Desorientering/förvirring: Verbala eller beteendemässiga symtom som tyder på att personen inte är orienterad till tid och rum eller förväxlar en person med en annan eller feltolkar personerna i omgivningen.
   b) Inadekvat beteende: Inadekvat beteende i relation till situationen; tex personen drar ut kanyler, katetrar eller tar bort förband eller försöker ta sig ur säng när det är kontraindicerat.
   c) Inadekvat kommunikation: Inadekvat kommunikation i relation till situationen; tex osammanhängande, obegripligt eller meningslöst tal.
   d) Illusioner/ hallucinationer: Ser eller hör saker som inte existerar; feluppfattning/misstolkning eller förvanskning av synintryck.
   e) Psykomotorisk förlångsamning: Fördröjd reaktion, få eller inga spontana reaktioner/ eller svar; till exempel när man stimulerar patienten får man ingen reaktion (oväckbar) och/ eller reaktionen är mycket fördröjd
3. Hur man kodar de fem symtomen:

0= symtomet förekommer aldrig under skiftet
1=symtomet förekommer under någon del av skiftet, men av lindrig grad
2= symtomet förekommer under någon del av skiftet, och var mycket uttalade eller störande

Datum																					
Arbetspass:	**D**	**K**	**N**	**D**	**K**	**N**	**D**	**K**	**N**	**D**	**K**	**N**	**D**	**K**	**N**	**D**	**K**	**N**	**D**	**K**	**N**
Desorientering																					
Inadekvat beteende																					
Inadekvat kommunikation																					
Illusioner/ hallucinationer																					
Psykomotorisk förlångsamning																					
Summa																					

D= dagpass (8-16), K= kvällspass (13-21), N= nattpass (21-07)

Utvecklad och baserad på forskning om delirium bland patienter med höftfraktur, Confusion Rating Scale (CRS) av M. A. Williams et al, 1988, förnyad version av Gaudreau et al 2005. Översatt till svenska av B Olofsson & Y Gustafson 2008.