Prehospital transportation, management, and outcome of cardiogenic shock in Northern Norway

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Abstract

Introduction: This study aimed to determine the impact of prehospital management and transfer to a tertiary hospital on the outcome of cardiogenic shock in a rural/urban setting.

Methods: Patients treated for cardiogenic shock in the period of 01.01.2019 to 31.12.2021, were retrospectively analysed with regards to transportation route, time to definite treatment, prehospital and intrahospital treatment, and outcome (mortality). Patients were anonymously recorded in a structured case report and analysed using SPSS.

Results: 83 consecutive patients were included in two cohorts; 34 patients were admitted directly to the tertiary care centre and 49 were referred from other healthcare services. Cohorts were analysed with regards to differences in therapy and outcomes. Mortality was higher in the direct cohort (74% vs. 34% at discharge, p. 0,001). Factors associated with mortality were increasing age and hypertension, deviating pH, BE and lactate- values, as well as severe cardiovascular disease upon admission.

The most common cause of shock was acute myocardial infarction (45%). The groups differed significantly in underlying aetiologies of shock, with higher incidence of out-of- hospital cardiac arrest (OHCA) in the direct transfer cohort (15 vs. 5 pt., p. <0.001), and decompensated heart failure (p. 0.006), cardiomyopathies and NSTEMI in the indirect transfers.

Patients in the transferred cohort had a median patient delay in contacting health services of nearly 14 hours (8 vs. 830 minutes, p. <0,001). The transferred cohort also took longer to receive definite treatment after contacting health services, on average 2,7 hours longer than the direct group (139 minutes vs. 303 minutes, p. <0,001). Time to treatment was not a predictor of mortality. Overall use of PCI in the population of 64%, 73% in the direct cohort compared to 55% in the indirect transfer cohort. There was a low usage rate of thrombolysis overall (15 patients, 19%), with little variance between the groups. There was similar usage of supportive treatment (ECMO, IABP) between the groups. Direct transfer patients had an average hospitalization of 3,5 days compared to 15 in the indirect transfers (p. 0,028)

Conclusion: Direct admission and transfers emerge as two distinct cohorts in our cardiogenic shock population. These groups had significant different aetiologies, different course of disease, partly different treatments, and somewhat different outcomes. This will be a basis for designing a new pre- and intrahospital treatment algorithm for our “hub and spoke-network”.

Introduction:

Cardiogenic shock (CS) is a low cardiac output state caused by cardiac dysfunction of various aetiologies, resulting in end organ hypoperfusion and hypoxia. The most common cause is acute myocardial infarction (AMI), accounting for approximately 80% of all instances of CS in industrial countries, with 5-12 % of all AMI being complicated by CS. Other causes include acute decompensated heart failure (1), which may account for up to 30% of cases depending on the population, and postcardiotomy shock, i.e. shock after cardiac surgery (2, 3). Current evidence and clinical practice guidelines support immediate revascularization of the infarct-related coronary artery as the primary therapy for cardiogenic shock following acute myocardial infarction(3, 4).

Historically, CS has been a condition with a severe mortality rate upwards of 80%(5). With the introduction of thrombolysis and early revascularization (PCI) the rate in AMI-CS remains around 50%. Both these treatments rely on timely intervention, with decreasing effectiveness the longer after onset of MI they are instituted (6).

Here we report on the handling and outcome of patients with CS in the setting of a sole tertiary hospital centre in the health region of Northern Norway ("Helse-Nord"), a heath region covering an area of approximately 112 951 square km, and 485 362 inhabitants (7, 8). It also serves the 70 925 square km of the Svalbard archipelago. This region is plagued by challenging weather conditions causing difficulties with interhospital transports with ambulances, fixed wing-planes, and helicopters. Except for a few small and mid-sized towns, the population is largely spread in rural areas (fig 1).

The University Hospital of Northern Norway (UNN) is the tertiary hub for a cardiogenic shock network and the only hospital in the region offering coronary angiography and PCI on a 24-hour basis. It also has an established ECMO-program (extracorporeal membrane oxygenation), cardiac surgery and operates a dedicated cardiac intensive-care unit.

The overall aim of our study was to determine if allocation to the pre-hub management and subsequent transfer to the tertiary hospital is somewhat a marker on the outcome of cardiogenic shock in our population. The primary outcomes of our interest are in-hospital deaths and both 30-day and 6-month mortality post discharge. Also, we did examine if there is a difference in choice of treatment based on expected travelling time.

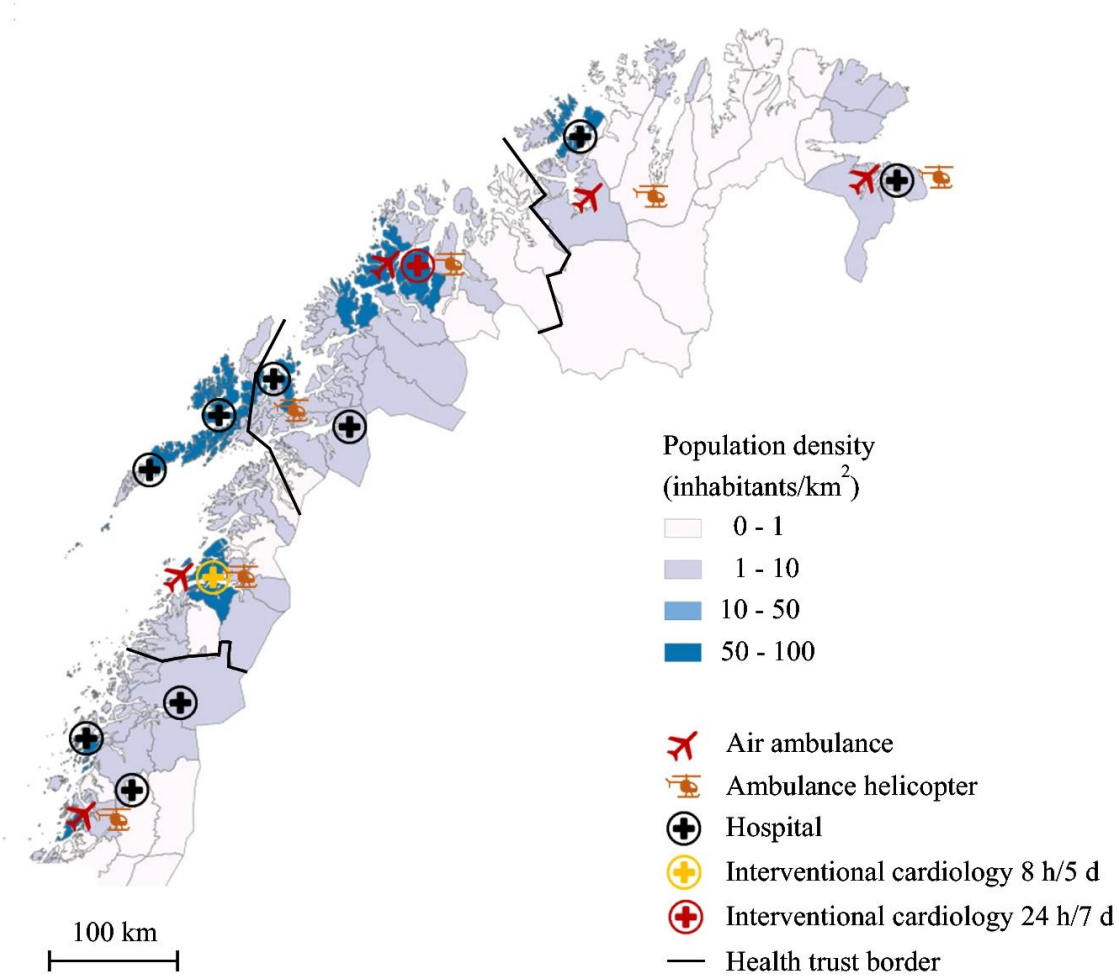

Figure 1: Area covered by the Northern Norway Regional Health Trust (excluding Svalbard archipelago), with 11 somatic acute care hospitals. Air ambulance bases are shown. The population density is depicted for each municipality. There are 26 operative airports in the area (not shown). Svalbard has its own rescue helicopter, airport, and acute care hospital. Figure from "The Barriers to Rapid Reperfusion in Acute ST-Elevation Myocardial Infarction" by Bartnes et al. (9).

Material and methods:

Patients were identified retrospectively through a targeted search of the electronic medical database (EPJ) at UNN Tromsø of patients who received the ICD-10-CM Diagnosis Code R57.0 of cardiogenic shock during their admittance. The search was limited to the period 01.01.2019 to 31.12.2021. The resulting patient list was and saved on an encrypted area of the hospitals data servers. The search yielded 140 patients. Exclusion criteria were age <18 or >90 (5 pt.), or admission for elective heart surgery (12 pt.). Duplicates (18 pt.), patients who did not meet the definition of cardiogenic shock (19 pt.), or who did not provide informed consent (3 pt.) were excluded from the survey. In total, we analysed 83 consecutive patients admitted UNN for cardiogenic shock in this 3-year period.

Data from included patients were extracted from the EPJ at UNN Tromsø, as well as the EPJ of other hospitals in Northern Norway and the prehospital emergency informational system (AMIS). We extracted patient demographics and prior medical history relevant to cardiac disease. Prehospital and intrahospital treatments were registered, as well as results of laboratory test, blood pressure values and echocardiography results. The patient cohort included all cases of CS, regardless of underlying cause or whether apparent upon admission or developed during hospitalization.

Missing or uncertain data: Missing data was left blank, and calculations based on registered entries. In instances impossible to determine exact time of events, such as debut of symptoms, the time was set to 12:00 of the given date of debut or to the nearest whole hour of debut.

Ethics: The study and data collection were approved by the Data protection official at UNN (Personvernombudet, PVO) and the Regional Committee for Medical and Health Research Ethics (REK), with the stipulation that surviving patients be informed of the study and given the opportunity to turn down the request to use their medical data in the survey (ref. 126549). All survivors were contacted by informational letters to their registered addresses, with return envelopes if consent was not given. We did not require consent from deceased patients next-of-kin.

Cardiogenic shock - definition:

Cardiogenic shock was defined as a cardiac dysfunction with persistent (> 30 min) low systolic blood pressure (< 90 mmHg), or the need to use inotropes/pressor and/or mechanical support to keep blood pressure above 90 mmHg. In addition to one or more signs of systemic hypoperfusion:

- Anuria, oliguria < 0,5 ml/kg/t.
- Cold extremities.
- Altered mental status.
- Increase in lactate > 2,0 mmol/L.

An overall assessment was used in patient with known HT and significant symptoms of hypoperfusion with higher measured blood pressure than 90 systolic.

Statistical analysis:

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 27.0. (Armonk, NY: IBM Corp). Continuous variables normally distributed were expressed as a mean with standard deviation and analysed using Student´s T-test. Continuous variables not normally distributed were expressed as a median with interquartile range and analysed using Mann-Whitney U-test. Categorical variables were expressed as numbers with percentages and analysed using Chi-square or Fishers exact where appropriate, using univariate analysis. When presenting data, the numbers were rounded to the nearest whole value. Multivariable analyses were not done due to the low number of patients included.

Results:

In 83 registered patients with cardiogenic shock admitted during the three-year period at UNN, 34 were transported directly to the hospital from the local primary care area (direct admittance). 49 patients were seen in an outside ER or treated at a local hospital before transfer to UNN (indirect admittance). In the indirect cohort 31 patients were first seen in an outside local hospital, and 18 were seen by primary physicians in family offices or emergency rooms.

Mortality:

Overall, in-hospital mortality rate was 52%. Factors associated with increased mortality were increasing age (61 vs. 70 years at 30-day mortality, p. 0,001), as well as hypertension (12 vs. 29 pt at 30-day mortality, p. 0,009). Other baseline factors were not related to mortality (table 2). Direct admission to UNN was associated with increased mortality (74% vs 41% at 30-days, p. 0.011).

This mortality difference between the two cohorts continued through the follow-up period but was not significant at the 6-month mark. We observed that all directly admitted patients succumbed while admitted, while 32% of fatalities in the indirect admittance group died during hospitalization.

Table 1: Mortality and outcome

	Total population, n = 83	Direct admittance, n=34	Indirect admittance * n=49	P-value
Dead during stay, n (%)	42 (51)	25 (74)	17 (35)	**< 0.001**
Dead 30 d	45 (54)	25 (74)	20 (41)	**0,011**
Dead 6 months	52 (63)	25 (74)	25 (51)	0,079
Discharged to home	21 (25)	6 (18)	15 (30)	0,298
Discharge to rehab	4 (5)	2 (6)	2 (4)	0.084
Discharge to other hospital	16 (19)	1 (3)	15 (30)	**0.030**

**Indirect admittance: Transfers from primary hospitals or patients referred from emergency rooms or primary care physicians*

Demographics:

Overall characteristics were similar in the two cohorts. There was higher incidence of atrial fibrillation in the indirect admittance cohort (15% vs. 3,8%, p. 0,045) and all registered strokes were in this cohort (8,8% vs. 0%, p. 0,017). No other differences were found between the cohorts (table 2).

Table 2: Patient characteristics

	Total population, n = 83	Direct admittance, n=34 (range, %)	Indirect admittance, n=49 (range, %)	P-value
Age, years (range)	66 (21-89)	66 (35-89)	66 (21-86)	0,784
Male, n (%)	59 (71)	23 (68)	36 (73)	0,279
Female, n (%)	24 (29)	11 (32)	13 (27)	
BMI, (kg, range)	28 (15-40)	27 (20-37)	28 (15-40)	0,228
Smoker, n (%)				
Current	24 (29)	11 (32)	13 (27)	0,336
Previous	40 (48)	27 (79)	34 (69)	0,207
Living at home, no assistance, n (%)	70 (84)	29 (85)	38 (78)	0,377
Prior medical history, n (%)				
Chronic HF	16 (19)	4 (12)	11 (22)	0,138
Myocardial infarction	16 (19)	7 (21)	9 (18)	0,468
Angina	11 (13)	5 (15)	6 (12)	0,541
Paroxysmal AF	15 (18)	3 (9)	12 (25)	**0,045**
ICD	5 (6)	2(6)	3(6)	0,570
Claudication	3 (4)	1 (3)	2 (4)	0,613
DVT/thrombosis	6 (7)	1 (3)	5 (10)	0,186
Hypercholesterolemia	17 (21)	6 (18)	11 (22)	0,532
Atherosclerosis	8 (10)	5 (15)	3 (6)	0,203
Hypertension	41 (51)	16 (47)	25 (51)	0,338
Cerebrovascular disease	7 (8)	-	7 (14)	**0,015**
COPD	8 (10)	2 (6)	6 (12)	0,359
Renal failure	15 (18)	4 (12)	11 (22)	0,195
Diabetes	34 (41)	12 (35)	22 (45)	0,242

Cardiomyopathy	3(4)	-	3 (6)	0,185
Previous PCI	19 (23)	8 (24)	11 (22)	0,592
Previous CABG	8 (10)	2 (6)	4 (8)	0,359

*BMI = body mass index, HF = heart failure, AF = atrial fibrillation, DVT = deep vein thrombosis, ICD = Implantable cardioverter-defibrillator, COPD = Chronic obstructive pulmonary disease, PCI = percutaneous coronary intervention, CABG = Coronary artery bypass graft surgery. *Values are rounded to nearest whole number*

Diagnosis at admission to tertiary hospital:

The cause of admission to the tertiary hospital was in most instances acute myocardial infarction (STEMI or NSTEMI, 37 pt., 45%). The second most common cause was prehospital cardiac arrest with obtained ROSC (20 pt, 24%). The remaining patients were admitted due to acute coronary syndrome without criteria for myocardial infarction (unstable angina with rapid deterioration), worsening heart failure and decompensated cardiomyopathies. Nine patients had other causes of admission complicated with CS in the course of the disease process (table 3).

Most cardiac arrests were found in the group of patients admitted directly to UNN (15 vs. 5 pt., p. <0.001), while all nine decompensated heart failure patients were transferrals through primary doctors or hospitals (p. 0.006). This was also the case for the cardiomyopathies (4 pt., p. 0,078). There were also a higher number of patients with NSTEMI in the transferrals (7 vs 1 pt., p. 0,070).

Table 3: Diagnosis upon admission at UNN

	Total population, n=83 (%)	**Direct admittance, n=34 (%)**	**Indirect admittance, n=49 (%)**	**P-value**
STEMI	29 (35)	14 (41)	15 (30)	0,224
Non-STEMI	8 (10)	1 (3)	7 (14)	0,072
Cardiac arrest with ROSC	20 (24)	15 (44)	5 (10)	**<0,001**
Decompensated HF	9 (11)	-	9 (18)	**0,005**
Cardiomyopathy	4 (5)	-	4 (8)	0,103
ACS	4 (5)	1 (3)	3 (6)	0,672
Other*	9 (10)	3 (9)	6 (12)	0,536

*STEMI = ST-elevation myocardial infarction, ROSC = return of spontaneous circulation, HF = heart failure, ACS = acute coronary syndrome. *Other: Methamphetamine induced cardiomyopathy (1 pt.), pulmonary oedema (2 pt.), atrial fibrillation (2 pt.), myocarditis (2 pt.), endocarditis (2 pt.)*

Tertiary centre treatment:

When examining the definite treatment, there was an overall usage of PCI in the population of 64%, 73% were treated with PCI in the direct cohort compared to 55% in the indirect transfer cohort. There was a low usage rate of thrombolysis overall (15 patients, 19%), with little variance between the groups. Thrombolysis was administered approximately equally in the prehospital setting (7 patients, 8%) and in-hospital. Only two patients received rescue PCI following thrombolysis. There was no statistical difference in usage of PCI, thrombolysis, or cardiac surgery between the cohorts.

25 (30%) of CS patients received ECMO treatment. Most received ECMO due to cardiac arrest (9 patients, 32%) and/or STEMI (8 patients, 32%). Most patients were direct referrals (14 patients, 58%, p. 0,052), or referrals from primary hospitals (7 patients, 29%). These patients were younger (62 vs. 68 years, SD 3, 95% CI: -12,9 - -0,3, p. 0,04), had worse troponin-T (17354 vs. 6782 ng/L, SD 3659, 95%

CI: 3279 – 17863, p. 0,005) and CK-values (4605 vs. 2069 U/L, SD 1048, 95% CI: 440 – 4630, p.0,018,) on average, as well as creatinine (239 vs 185 µmol/L, SD 30, 95% CI: 5,7 – 12, p. 0,032) compared to the overall population.

Hospital mortality was 63%, 6-month mortality wase 71% in the ECMO cohort. The patients treated with ECMO had longer hospitalizations (26 vs. 10 days, SD: 6,9, 95% CI: 2-29, p. 0,025) and longer ICU treatment (19 vs. 6 days, SD 3,7, 95% CI: 5,7 – 20,3, p. <0,001) and ventilation (14 vs 4 days, SD 4,6, 95% CI: 0,8 – 19,5, p. 0,033). They had higher prevalence of cardiac surgery in the course (1 vs 6 patients, p. 0,003), IABP usage (8 vs. 9 patients, p. 0,025), and ventilator treatment (23 vs. 23 patients, p. <0,001). There was no association between duration of ECMO- and ventilator-treatment and mortality.

Survivors had on average 13 days longer admissions than non-survivors (15 vs. 2 days, p. < 0,001) and had longer admissions to the ICU (6 vs. 2 days, p. 0,003). The direct cohort had significantly shorter hospitalizations, related to their higher intrahospital mortality (median treatment time 3,5 days vs.13,5 days, p. 0,028). There was no significant difference in ICU-treatment time, ECMO or ventilation time between the groups. There was no statistical difference between the cohorts in usage of supportive treatments or pressors/inotropes. The need for vasopressors (noradrenaline or adrenaline) was associated with mortality (p. 0,049 and <0,001 respectively).

Table 4: Treatment given at tertiary centre, and treatment duration.

Admission*	**Total population, n=83 (SD, %)**	**Direct admittance, n=34 (SD, %)**	**Indirect admittance, n=49 (SD, %)**	**P-value**
Treatment				
PCI	52 (64)	25 (74)	27 (55)	0,112
Thrombolysis	15 (19)	7 (21)	8 (16)	0,468
Cardiac surgery	7 (8)	3 (9)	4 (8)	0,333
Supportive treatment				
IABP	16 (19)	7 (21)	9 (18)	0,564
ECMO	24 (29)	14 (41)	10 (20)	0,052
Dialysis	11 (13)	5 (15)	6 (12)	0,541
CPAP/BiPAP	38 (46)	14 (41)	24 (49)	0,359
Mechanical ventilation	44 (54)	22 (65)	22 (45)	0,101
Vasopressors				
Dopamine	3 (4)	-	3 (6)	0,185
Dobutamine	55 (66)	22 (64)	33 (67)	0,334
Noradrenaline	60 (72)	26 (76)	34 (69)	0,503
Adrenaline	16 (20)	9 (26)	7 (14)	0,168
Diuretics	50 (61)	21 (62)	29 (59)	0,545
Morphine	53 (65)	23 (68)	30 (61)	0,506
Nitrates	8 (10)	1 (3)	7 (14)	0,072
Hospitalization, days	10 (SD 30)	3,5 (SD 41)	13,5 (SD 18)	**0.028**
Days in ICU	5 (SD 15)	4,5 (SD 10)	5 (SD 18)	0,922
Days on ventilator	4 (SD 16)	4 (SD 9)	4 (SD 20)	0,503
Days on ECMO	4 (SD 5)	5 (SD 5)	4 (SD 5)	0,899

*PCI = percutaneous coronary intervention, IABP = Intra-aortic balloon pump, ECMO = extracorporeal membrane oxygenation, CPAP = continuous positive airway pressure, BiPAP = bilevel positive airway pressure, ICU = intensive care unit. *Admission data expressed as median.*

Cardiogenic shock

CS was present upon admission in 57% of patients. The development of shock after admission occurred mostly in the first 6 hours. Shock upon admission were more prevalent in the direct cohort (65%), and all patients in this cohort developed shock within the first 24 hours following admission. We observed a group of patients also developing shock late in the treatment course, defined as over 48 hours following admission. These late presentations were commonly due to decompensation of HF or cardiomyopathies or complications following given treatment, and all were in the transferred cohort. Timing of shock development was not directly associated with mortality.

Worst systolic blood pressure in shock duration was correlated with increased mortality (57 mmHg vs 68 mmHg, p. 0,007). Pulse and symptoms present upon development of shock had no correlation with mortality. More patients were unconscious upon presentation of CS in the direct cohort (18 vs. 9 pt., p. 0,002), other symptoms were evenly distributed among the cohorts.

Table 5: Debut of cardiogenic shock

	Total population, n=83 (%)	**Direct admittance, n=34 (%)**	**Indirect admittance, n=49 (%)**	**P-value**
At admission*	46 (57)	22 (65)	24 (49)	0,139
CS debut during hospitalization:	37 (44)	12 (35)	25 (51)	0,101
First 6 h	23 (28)	11 (32)	11 (22)	0,209
First 12 h	2 (3)	-	2 (4)	0,328
First 24 h	5 (6)	1 (3)	4 (8)	0,288
24-48 h	1 (1)	-	1 (2)	0,672
>48 h	7 (8)	-	7 (14)	**0,043**

*CS = cariogenic shock. *At admission to tertiary centre*

Table 6: Symptoms present at debut of cardiogenic shock.

	Total population, n=83 (%)	**Direct admittance, n=34 (%)**	**Indirect admittance, n=49 (%)**	**P-value**
Tachycardia	22 (27)	7 (21)	15 (31)	0,175
Bradycardia	10 (12)	4 (12)	6 (12)	0,558
Impaired consciousness, confusion	33 (40)	13 (38)	20 (41)	0,406
Unconscious	28 (34)	18 (53)	10 (20)	**0,002**
Oliguria/anuria*	43 (52)	15 (44)	28 (57)	0,104
Pale	24 (29)	8 (24)	15 (31)	0,263
Cold skin	54 (65)	21 (62)	33 (67)	0,387
Cyanosis	19 (23)	8 (24)	11 (22)	0,592
Dyspnoea	34 (41)	13 (38)	21 (43)	0,333
Mean MAP at debut**	62 (27-102)	60 (40-95)	63 (27-102)	0,781

Mean MAP, worst clinical	48 (17-83)	47 (17-73)	49 (27-83)	0,452
Systolic BP at debut of CS, mmHg	81 (40-130)	81 (55-125)	82 (40-130)	0,623
Worst systolic BP in duration, mmHg	63 (20 - 110)	62 (20-90)	64 (30-110)	0,501
Pulse at debut CS	93 (20 - 110)	90 (35-150)	92 (20-180)	0,862
Worst pulse at CS (tachycardia or bradycardia)	105 (20 -105)	100 (23-180)	95 (20-230)	0,485

*MAP= mean arterial pressure, BP= blood pressure in mmHg. *Not reported in several patients with severe CS upon admission and short admissions. ** Values are expressed as mean and range.*

Prehospital course of disease and treatment

The cohorts differed significantly in patient delay in contacting health services, as patients in the indirect transfer cohort had a median patient delay of nearly 14 hours (8 vs. 830 minutes, p. <0,001). The transferred cohort also took longer to receive definite treatment after contacting health services, on average 2,7 hours (139 minutes vs. 303 minutes, p. <0,001). All coronary patients in the cohort were classified as rescue-PCI. They also took significantly longer time to admission to our tertiary hospital (114 vs. 334 minutes, p. 0,001), although the time to admission at a primary hospital were 111 minutes, making the time before examination by a physician similar in the cohorts. We also observed that the patients who were in the direct cohort and received thrombolysis did so in a shorter time span than the ones in the transferred cohort (65 vs. 83 minutes), although the difference was not significant.

Even with these major differences in transport time between the cohorts, the time to treatment was not a predictor of mortality. Direct transport to our tertiary centre was associated with increased mortality at all recorded timepoints (27 vs. 9 patients at 30 days, p. 0,003), and reversely we observed increased survival in patients transferred from primary hospitals (20 vs. 10 patients, p. 0,002).

Prehospital treatment was not associated with mortality, nor were primary hospital treatment. More patients received AHLR in the direct group compared to the indirect group (11 vs. 4 pt, p. 0,008), intubation (10 vs. 4, p. 0,017), as well as LUCAS-based resuscitation (6 vs. 1 pt, p. 0,016). There was no difference in administration of pressors/fluids in the prehospital setting between the groups.

Table 7: Transport data

	Total population, median (range)	**Direct admittance, Median (range)**	**Indirect admittance, Median (range)**	**P-values**
Symptom debut to contact with health services, minutes	60 (0-8066)	8 (0-450)	830 (0-8066)	**<0,001**
After contact with health services, minutes:				
Time to primary hospital	101 (0-225)	-	111 (48-368)	
Time to tertiary hospital	182(30-13140)	114 (30-313)	334 (95-13140)	**<0,001**
Time to PCI, minutes	220 (37-4485)	139 (37-2895)	374 (115-4485)	**<0,001**
Time to thrombolysis, minutes	78 (46-368)	65 (46-165)	83 (48-368)	0,355

Ambulance	21 (25)	11 (32)	10 (15)	0,226
Helicopter	38 (50)	22 (65)	16 (25)	**0,009**
Plane	24 (30)	3 (9)	22 (34)	**<0,001**

Table 8: Survival based on transport route.

Transport to tertiary centre:	Total population, n=83(%)	Alive 30-days, n=38 (%)	Dead 30-days, n=45 (%)	P-value
Directly	34 (41)	9 (23)	25 (55)	**0,003**
Indirectly	49 (59)	29 (76)	20 (44)	0,003
From primary hospital	31 (37)	20 (52)	10 (22)	**0,002**
From urgent care centre	12 (14)	4 (10)	8 (18)	0,325
From family doctor	12 (14)	5 (13)	6 (13)	0,589
Both emergency care and primary hospital	13 (16)	8 (21)	5 (11)	0,125

Table 9: Prehospital treatment

	Total population, n=83 (%)	Direct admittance, n=34 (%)	Indirect admittance, n=49 (%)	P-value
None	9 (12)	2 (6)	7 (14)	0,169
MONA	19 (25)	11 (32)	8 (16)	0,100
Morphine	27 (33)	13 (38)	14 (29)	0,316
Oxygen	53 (70)	27 (79)	26 (53)	**0,022**
Nitro-glycerine	28 (34)	12 (35)	16 (32)	0,584
ASA	30 (40)	13 (38)	17 (25)	0,394
Diuretics	3 (4)	-	3 (6)	0,183
Fluids	18 (24)	7 (21)	11 (22)	0,464
CPAP	5 (7)	3 (9)	2 (4)	0,361
Respirator	14 (18)	10 (29)	4 (8)	**0,017**
Inotropes/Vasopressors	10 (13)	6 (18)	4 (8)	0,198
LUCAS	7 (9)	6 (18)	1 (2)	**0,021**
Thrombolysis	7 (9)	5 (15)	2 (4)	0,113
AHLR	15 (20)	11 (32)	4 (8)	0,008

Table 10: Primary hospital treatment

	31 (%)	Alive 30-days	Dead 30-days	P-value
MONA	13 (46,4)	8 (28,6)	5 (17,9)	0,396
Inotropes/vasopressors	15 (53,6)	9 (32,1)	6 (21,4)	0,293
Thrombolysis	4 (14,3)	4 (14,3)	-	0,189
Fluids	16 (57,1)	10 (35,7)	6 (21,4)	0,388
NIV/CPAP	3 (10,7)	2 (7,1)	1 (3,6)	0,704
Respirator	3 (10,7)	3 (10,7)	-	0,296

28 patients were treated at primary hospital before transfer to tertiary hospital. 3 patients transferred without receiving definite treatment at primary hospital.

Lab values:

Lactate (5,2 vs. 10,2 mmol/L, p. 0,003), pH (7,26 vs. 7,14, p. 0,015) and BE (-10 vs. -16 mmol/L, p. 0,004) were all associated with increased mortality. More severe cardiovascular disease at angiography were associated with increased mortality, defined as 3-vessel disease (5 vs. 18 pt., p. 0,015) and main stem stenosis (1 vs. 8 pt., p. 0,044). Overall, laboratory measurements were comparable between the cohorts, aside from lower pH measured in the direct group (7,1 vs 7,2, p. 0,027).

Table 11: Worst lab values during CS

	Total population, median (range)	Direct admittance, Median (range)	Indirect admittance, Median (range)	P-value
eGFR, mL/min/1,73 m2, lowest	32 (7-109)	43 (7-109)	36 (8-109)	0,528
Lactate, mmol/L, highest	7,1 (1,1-24)	8,8 (1,4 - 24)	6,6 (1,1 -20)	0,532
pH, lowest	7,2 (4,5-7,4)	7,1 (4,5-7,3)	7,2 (6,7-7,4)	**0,027**
BE, mmol/L, lowest	-13 (-26-0)	-14 (-26 - 0)	-12 (-25 - -1)	0,571
Troponin-T, ng/L, highest	4443(23-72283)	5328 (34-72283)	4049 (23-54399)	0,361
CK, U/L, highest	1565 (53-25429)	1618 (53-25429)	1227 (136-7497)	0,340
Na at debut, mmol/L	138 (116-148)	137 (116 - 148)	137 (116 - 147)	0,535
K at debut, mmol/L	4,5 (2,9-7,3)	4,5 (2,9-7,3)	4,7 (3-7,2)	0,569
CRP, mg/L, highest	156 (0-453)	209 (0-453)	153 (0-421)	0,180
Creatinine, µmol/L, highest	177,00 (51-690)	167 (51-690)	207 (62-547)	0,405
Hb at debut, g/dL	13,1 (8,2-21,9)	13 (8,2-21,9)	12,9 (8,7-17,3)	0,919

eGFR= Estimated globular filtration rate, BE = base excess, CK = creatine kinase, K = potassium, Na = sodium, CRP = C-reactive protein. As values were not normally distributed, values are expressed as median, and analysis done using Mann-Whitney U-test.

Procedures at tertiary hospital:

3-vessel and left main stem coronary disease were associated with increased mortality (5 vs. 18 pt., p.0,015 and 1 vs. 8 pt., p. 0,044, respectively). There were more patients not undergoing angiography in the transferred cohort (11 vs. 1 pt, p. 0.008), due to other aetiologies than myocardial infarction. In those patients undergoing angiography in the two groups, there was no significant difference in vessel pathology.

Table 12: Diagnostic procedures at tertiary hospital

	Total population, n=83 (%)	Direct admittance, n=34 (%)	Indirect admittance, n=49 (%)	P-value
Chest X-ray	65 (80)			
Congestion	28 (43)	8 (24)	20 (41)	0,121
Pulmonary oedema	21 (31)	10 (29)	11 (22)	0,218
Echocardiography at admission	77 (95)			

EF <30	53 (67)	22 (65)	31 (63)	0,397
EF 30-50	19 (26)	11 (32)	8 (16)	0,189
EF >50	4 (5)	1 (3)	3 (6)	0,406
Angiography				
Performed, n (%)	76 (95)	33 (97)	35 (71)	**0,008**
1-vessel	21 (27)	10 (29)	11 (22)	0,362
2-vessel	12 (15)	5 (15)	7 (14)	0,335
3-vessel	24 (30)	11 (32)	13 (27)	0,518
Main stem stenosis	9 (12)	3 (9)	6 (12)	0,495
Intracoronary thrombi	17 (22)	9 (26)	8 (16)	0,208
Normal	14 (18)	6 (18)	8 (16)	0,578

Discussion:

***Organization of shock treatment in northern Norway**:*

In recent years there has been an increasing focus on establishing solid regional systems for management of CS. It is proposed that to improve mortality it is important to establish a network of care and routines for CS in much the same way as such systems have been established for other high mortality conditions such as STEMI, OHCA and stroke. CS treatments have traditionally been included as a subgroup under these systems (STEMI and OHCA primarily)(3).

An important requirement for a CS network is a hub or centre providing a set of advanced treatments like a 24/7 interventional cardiology service (PCI), intensive care facilities with mechanical ventilation, advanced shock-treatment staff skills, renal replacement therapy, cardiac surgery, and circulatory support systems like short- and long-term mechanical assist systems (3). In the health region of northern Norway such a centre is placed in Tromsø. The particular geographic challenges for organizing a cardiogenic shock network lies in a vast scarcely populated area with challenging weather condition for a large part of the year. Thus, the time frame and transport models to be developed are often unique in both a national and international context.

Transport to the regional centre in Tromsø rely heavily on air transportation between local community hospitals and the centre, as described in our material. Even with a dense air evacuation system using both helicopters and planes, this forces long evacuation times, and a demand for local primary stabilization and treatment.

It is postulated that the establishment of systems of care with high volume hospitals used as hubs integrated with emergency medical systems and spoke centres with clearly defined protocols for early recognition, management and transfer have the potential to improve patient outcomes (3). The proposed model is an “hub-and-spoke” model, with tight cooperation between primary hospitals and emergency services in recognizing CS, with the aim of local stabilization of patients before fast transfer to a tertiary centre with specialized competence in this condition and competence in reperfusion of coronary pathology and advanced support therapy. A potential addition is a mobile «CS-team» (11), with the opportunity to support primary hospitals on-site for treatment and stabilizing of patient before transfer to the tertiary centre. Variants of such a “hub-and-spoke model” have been stablished in densely populated areas like New-York and Metropolitan Paris with an apparently positive impact on survival rate (11, 12). Our present report is part of an effort to apply transferrable aspects of such a model to the geographical distances and rural setting of northern Norway, and thus hopefully saving patients who presumably die in the primary setting today.

Cohort characteristics

Some distinctions emerged between our two cohorts upon examination. Cause of admission differed, with a significantly higher incidence of cardiac arrests in the patient admitted from the local area of UNN, owing to the pre-existing treatment algorithms for OHCA – where fast transport and time limits for institution of treatment is established in protocols (12). Reversely, there were more patients suffering NSTEMI, and CS due to other conditions than myocardial infarction, i.e., heart failure and cardiomyopathies, in the transferred group. Thus, apparently the transferred population reflects a selection process where patients with an acute grave clinical situation most probably never reach the evacuation chain, but the more prolonged and insidious shock syndromes are referred when the shock-spiral escalates (13, 14).

We observed that the patients who were transferred had much longer patient delay before contacting health services and had better pH during the course. This may suggest less rapid pathophysiological deterioration in this group. This less rapid deterioration in the indirect group may largely be attributed to patients suffering shock due to other aetiologies than myocardial infarction. We know that that the patients suffering shock due to heart failure (CS-HF) instead of the more common myocardial infarction, more commonly have a drawn-out course with marginal function over time before derailment into CS (13)(15).

The overall difference between the two groups is also reflected in a higher incidence of late shock development in the transferred group. This can probably be attributed to the high number of patients suffering shock due to heart failure (CS-HF) as opposed to myocardial infarction and therefore have a drawn-out course with marginal function over time before deteriorating to CS (13-15). The time frame for shock development was not however a predictor of mortality.

Tertiary hospital treatment

There was no significant calculated difference in intrahospital treatment between the groups, although we did observe a higher overall usage of PCI in the directly admitted group (73% vs. 58%). PCI was more commonly used as a primary therapy in the direct cohort as these patients more often arrived in the Cath-lab within the guideline defined 120-minute window, compared to transferred patients where PCI was a rescue strategy in most patients (16, 17). When excluding patients with cardiomyopathies and decompensation of chronic heart failure from the cohorts, the PCI rate was 90%.

Overall, administered thrombolysis was similarly low in the groups. This is somewhat surprising as prehospital and early drug-based reperfusion should be the best opportunity for rapid revascularization is our geographically outstretched region. However, our data are in line with a detailed analysis of rapid reperfusion of acute ST-elevation myocardial infarction conducted in 2020 and 2021 showing that only 29% of 146 such patients had timely and early reperfusion (9).

Directly admitted patients had significantly shorter hospital stays reflecting their higher intrahospital mortality (median treatment time 3,5 days vs.13,5 days, p. 0,028). Patients who died during hospitalization had an average treatment duration of 2 days.

ECMO treatment was commonly due to OHCA or STEMI with established SCAI level D or E (18). The indication for ECMO treatment, both for cardiac arrest and cardiogenic shock, is controversial.

However, there is an increasing trend towards ECMO treatment internationally (19). The large randomized ECLS-Shock study did not observe an increased survival using an up-front early strategy for ECMO implantation, and further studies to clarify optimal selection of patients, ECMO set-ups and monitoring of organ effects are obviously warranted (20).

Mortality:

The overall mortality of 52% is in accordance with expected mortality when compared to publications from recent randomized trials (20) and registries (21). Since the documented value of early reperfusion of myocardial infarctions in 1999 (22) no substantial advances in therapy has been obtained. The last of several negative trial, the ECLS-Shock trial (20), could not demonstrate a beneficial effect of routine early application of ECMO treatment. Importantly, our present study points to the fact that the cardiogenic shock-population in a "rural hub-centre" consists of a heterogenous patient population with a broad range of pathologies and a "one-size-fits all" treatment option is not likely to be found.

We may postulate that the differences in mortality rate observed is attributed to the mentioned differences in underlying conditions, with a larger percentage of STEMI and OHCA patients in the direct cohort, conditions with traditionally higher mortality rates (17, 23, 24). Also, one of the factors associated with increased mortality in our material was more severe coronary disease upon admission (3-vessel or main stem). Patients with such severe cardiovascular disease are more liable to be transferred directly to PCI centres, given the established prehospital treatment algorithms for STEMI patients (16, 17). We did not observe such a correlation in our material, however. We also know that CS-related mortality in patients with CS-HF is lower than in CS caused my infarction, around 30%, explaining in part the lower observed mortality in the indirect cohort (14, 15)(2).

An important unknown factor is the number of patients dying of CS in the primary hospitals, and thus does not show up in our material. However, it is reasonable to expect some degree of selection where moribund or severely multimorbid patients may have been declined for further transport and treatment. It is also reasonable to expect that some patients die of CS before being admitted to any hospital, making it unlikely for the patients to be registered as such.

General morbidity.

Physiological factors found to be associated with increased mortality were lactate, BE and pH. These are well known biomarkers for the severity of shock (22). We also found the lowest measured systolic blood pressure and the need for inotropes to be associated with increased mortality. In patients with cardiovascular disease, we found more severe cardiovascular disease to be associated with increased mortality, here defined as three-vessel, or left main coronary artery disease(2).

Future directions

Two separate groups of CS emerged in our material, the patients with a rapid shock development, requiring direct transport to a shock centre and the group with a more drawn-out course, being treated in the primary hospital setting and being able to compensate the physiological processes for a while until ultimately developing shock. It is likely that when organizing a "hub-and-spoke" network in the future, we will need to establish two separate strategies to ensure effective treatment of both groups and improve outcomes in our region.

In the group with a rapid development, the effective recognition of (pre-) CS and rapid implementation of preventive measures to interrupt the pathophysiological spiral is important. Here, the improved usage of thrombolysis may help bettering outcomes, particularly in instances with longer travel time to tertiary care. Treatment of CS is otherwise limited for the prehospital workers, as ambulances does not carry pressors, only fluids. Air-ambulances carries pressors and often include an anaesthesiologist in the team. Therefore, it is also important to allocate appropriate resources to these patients.

We do not know enough about the transferred cohort, particularly the patients transferred from primary hospitals, to provide definite recommendations for future organization. It will be necessary to conduct a larger study examining the composition, and total incidence of CS in this group, as well as mortality.

A mobile CS-team working in this rural/urban setting with the geographical challenges may not be a wise use of resources. There will, however, be a need for improvements of several aspects of both organization and treatment. There should be an increased usage of prehospital thrombolysis, improve on communication between prehospital forces and tertiary hospitals with shock competence, and the organization of prehospital transport. It will require effective and tight interaction between several different health professionals to efficiently identify the patients who may benefit from advanced shock therapy and sort out patients with poor prognosis, for whom palliative care may be more appropriate. The improvement of cardiogenic shock therapy is likely a multifactorial process, where several processes must be implemented to reduce mortality and improve outcome.

Limitations:

The study is one small part of evaluating and improving the treatment for patients who develop cardiogenic shock in our region. We did only analyse the course for patients who were admitted to the tertiary care hub centre with CS to assess the results and challenges facing this institution. We do not know the prevalence of CS in the primary hospital setting. It would be interesting to do a study examining the transfer rate of patients for further treatment.

Due to the retrospective nature of the study, we also have no way of knowing if we did include all patients with CS in our study. We are dependent on the documentation present in the EPJ and other electronic patient data systems. It is possible that some patients suffering CS in the prehospital setting died before admission, without being coded as CS. We also have a relatively small population, making it hard to make any definite conclusions based on our results.

The study period included the Covid pandemic period occurring in our region from February 2020. This pandemic had an extensive impact on CS epidemiology and handling. Our recruitment and conduction of the EU-sponsored "Euroshock" – trial (25) was put on hold and ended with an aborted trial due to low recruitment throughout Europa. In a three-year period, we only had 101 adult patients (including CS in elective surgery and patients reserved from this study) suffering from CS at our centre, an average just shy of 34 patients a year. This is very low numbers for a tertiary shock centre, also compared with previous publication from our centre (26). The low number of patients hamper the possibility to do robust calculations and statistics, but we believe that our observations may serve as a benchmark for further assessment of the feasibility for CS treatment networks in the rural-urban setting.

Conclusion:

Patients transported directly to our tertiary centre had higher mortality rates despite less patient delay in contacting health services and faster transport to definite treatment compared to the patients transferred from primary hospitals and other primary health services. This difference is likely due to differences in underlying causes of shock development in the two groups.

Our study does not paint the whole picture, as there are likely patients dying of CS in the prehospital and primary hospital setting, patients we have not been able to include in our material. This project may, however, serve as a benchmark for the feasibility and organization of a CS network in our rural-urban setting. Future projects are necessary to determine the optimal organization of such a network.

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