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Title: Comparing ST-segment elevation myocardial infarction care between patients residing in central vs remote locations: a retrospective case series

Authors: Ahmad Kamona MSc (ahmad.kamona@nhs.net)[1], Scott Cunningham PhD (s.cunningham@rgu.ac.uk)[1], Brian Addison PhD (b.addison@rgu.ac.uk)[1], Gordon F Rushworth MSc (gordon.rushworth@nhs.net)[1,2], Andrew Call RGN (Andrew.call@nhs.net)[3], Charlie Bloe (charlie.bloe@nhs.net) RGN[3], Alistair Innes MRCP (alistair.innes@nhs.net)[4], Raymond R. Bond PhD (rb.bond@ulster.ac.uk)[5], Aaron Peace FRCP (apeace9@icloud.com)[6], *Stephen J Leslie FRCP (stephen.leslie@nhs.net)[3,7]

Affiliations: [1] School of Pharmacy & Life Sciences Robert Gordon University, Aberdeen, UK, AB10 7GJ. [2] Highland Pharmacy Education & Research Centre, Room D/509, Centre for Health Science, Old Perth Road, Inverness, UK, IV2 3JH. [3]Cardiac Unit, Raigmore Hospital, Inverness, UK, IV2 3UJ. [4] Dr MacKinnon Memorial Hospital, Broadford, Isle of Skye, UK, IV49 9AA. [5]School of Computing and Mathematics, Ulster University, Northern Ireland, UK, BT37 0QB. [6]Cardiac Unit, Altnagelvin Hospital, Glenshane Road Northern Ireland, UK, BT47 6SB. [7]Department of Diabetes & Cardiovascular Science, University of the Highlands and Islands, The Centre for Health Science, Old Perth Road, Inverness, UK, IV2 3JH.

***Author for correspondence:**

Professor Stephen J Leslie, Cardiac Unit, Raigmore Hospital, Inverness, IV2 3UJ, UK. Tel: ++44 1463 705459/62

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Abstract

Introduction

Patients who experience an ST-elevation myocardial infarction (STEMI) due to an occluded coronary artery require prompt treatment. Therapies to open a blocked artery are called reperfusion therapies (RT) and can include intravenous pharmacological thrombolysis (TL) or primary percutaneous coronary intervention (pPCI) in a cardiac catheterisation laboratory (cath lab). Optimal RT (ORT) with pPCI or TL reduces morbidity and mortality. In remote areas, a number of geographical and organisational barriers may influence access to ORT. However, these are not well understood and the exact proportion of patients who receive ORT and the relationship to time of day and remoteness from the cardiac cath lab is unknown.

Aims

To compare the characteristics of ORT delivery in central and remote locations in the North of Scotland and to identify potential barriers to optimal care with a view to service redesign.

Methods

The study was set in the North of Scotland. All patients who attended hospital with a ST elevation myocardial infarction between March 2014 and April 2015 were identified from national coding data. A data collection form was developed by the research team in several iterative stages. Clinical details were collected retrospectively from patients' discharge letters. Data included treatment location, date of admission, distance to the cath lab, route of access to health care, left ventricular function and RT received. Patients were described as *remote* if > 90 minutes driving time from the cardiac cath lab and *central* if ≤ 90 min drive time. For patients who made contact in a pre-hospital setting ORT was defined as pre-hospital TL or pPCI. For patients who self-presented to the hospital first, ORT was defined as inhospital TL or pPCI. Data were described as mean (SD) as appropriate. Chi-squared and Student's *t*-test were used as appropriate.

Each case was reviewed to determine if ORT was received and if not, the reasons for this were recorded to identify potentially modifiable barriers. Approval from the Caldecott guardian and Research and Development office were obtained but full ethical review was not required.

Results

Of 627 acute myocardial infarction patients initially identified, 131 had a STEMI, the others were a non-STEMI. From this STEMI cohort, 82 (62%) patients were classed as *central* and 49 (38%) were *remote.* In terms of initial therapy, 26 (20%) received pPCI, 19 (15%) received pre-hospital TLs, 52 (40%) received in-hospital TL, while 33 (25%) received no initial RT. ORT was received by 53 (65%) central and 20 (41%) remote patients; Chi-square = 7.05, DF =130, $p < 0.01$). Several recurring barriers were identified.

Conclusion

This study has demonstrated a significant health inequality between the treatment of STEMI in *remote* compared to *central* locations. Potential barriers identified include staffing availability and training, public awareness and inter-hospital communication. This suggests that there remain significant opportunities to improve STEMI care for people living in the North of Scotland.

Abstract word count 471

Introduction

Myocardial infarction (MI) continues to be a leading cause of death world wide[1]. According to the British Heart Foundation, in 2013-2014 there were 187,421 hospital visits in the UK due to MI which translates to someone in the UK having an MI every three minutes[2]. ST-segment elevation MI (STEMI) represents a high risk of early death and myocardial damage due to acute occlusion of a coronary artery[3].

Treatments to open a blocked coronary artery are called reperfusion therapies (RT) and include pharmacological thrombolysis (TL) that is administered intravenously[4] or primary percutaneous coronary intervention (pPCI)[5] performed in a cardiac catheterisation laboratory (cath lab). Optimal RT (ORT) with pPCI[6] or TL[7] given timeously (<120 min delay for pPCI and <30 mins for TL) reduces morbidity and mortality. However, if ORT is not delivered promptly then the risk of death is increased and left ventricular systolic impairment (LVSD) causing heart failure and an increase in mortality is more likely[8-10].

pPCI is the preferred RT (due to mortality and morbidity benefits)[11,12] although TL still has a role in the treatment of some patients due to the lack of availability of a cath lab within the recommended time frame[13]. The European Society of Cardiology guidelines suggest pPCI should be carried out within 120 minutes[14], if this is not possible then pre-hospital TL should be given. In practice this will translate to a maximum transfer time of 90 mins to a cath lab from start of symptoms. Patients who have a myocardial infarction diagnosed in the pre-hospital setting and are unable to get to a cath lab within the 90 min from the start of their symptoms should be given TL, otherwise immediate transfer to a pPCI facility should occur[11]. The delivery of TL in remote areas could therefore be considered the ORT.

However, the delivery of ORT in remote areas is not consistent[15] and barriers may exist including staffing (lack of paramedic crews), education and training (lack of

confidence to deliver prehospital TL) and equipment issues (unable to transmit ECG for telemetric support)[16]. By identifying modifiable and non-modifiable barriers to ORT and exploring the factors that might contribute to potential difference in clinical outcomes between *central* and *remote* patients, recommended strategies can be employed to try to overcome such barriers and mitigate the impact of remoteness in patient care. However, the exact proportion of patients who receive ORT and the relationship to time of day and remoteness from the cardiac cath lab is currently unknown.

This study aimed to investigate ORT delivery in a remote region in the North of Scotland in relation to location of STEMI and time of day and to identify potential barriers to optimal care.

Methods

Participants

Patients who had an STEMI during a 12 month period (March 2014 and April 2015) were included. Patients were identified from their final diagnosis code on discharge from hospital or death. Data from patients who died prior to attending hospital were not included.

Setting

The study was set in the North of Scotland (NHS Highland). This area represents 41% of Scotland's landmass (30,660 km²) with only 4% of the population (232,132)[17]. There are several hospitals in the area. The *regional centre* (Raigmore Hospital) is located in the south east and has a cath lab which operates during office hours (Mon-Fri, 08.30 to 18.00). There are three *rural hospitals* ('Broadford' in Skye, 'Belford' in Fort William, 'Caithness General' in Wick) which admit acute cases. Out of hours access to a cath lab is obtained from three *tertiary centres* (Aberdeen, Glasgow and Edinburgh) all > 90 min travel time.

Study design

This was a retrospective case series review.

Data collection and handling

The list of potential patients was obtained from the Scottish Morbidity Record (SMR), which includes date of admission/discharge and location of admission. SMR is an episode based record relating to all inpatients and day cases discharged from Scottish

hospitals. The inclusion criterion was any patient diagnosed with STEMI. Exclusion criteria included diagnosis of a non-STEMI, unknown diagnosis or living outside of the north of Scotland region. Further clinical details were obtained from the patients' discharge letters through Scottish Care Information (SCI) Store (a data repository which retains patient information at a health board level). Any missing information from patients discharge letters were obtained from other bespoke clinical reporting systems (echocardiography and PCI). Self-present patient data were obtained from the accident and emergency departments.

The primary outcome measure was whether ORT was received or not. Secondary outcome measures included death and LV function. The following data were obtained from case note review; age, gender, postcode, time of presentation, date of admission and discharge, treatment type and location, distance and travel time from cath lab and LV function.

The travel times via driving a car were obtained using Google Maps[18], although it should be noted that ambulance drive speed, road conditions and weather will impact on the actual drive times. Patients were described as *remote* if >90 minutes and *central* if ≤90 driving time from the regional centre. ORT was defined as the best possible RT for the specific patient at the specific time. Individualising ORT for each patient relied on several factors; drive time from the nearest cath lab, time and day of presentation, patient eligibility for PCI/TL and route of access to health care (e.g. self-presenters to hospital would not be eligible to receive pre-hospital TL). pPCI was considered ORT for all patients, while pre-hospital TL was considered ORT in all remote patients or central patients presenting out of 'cath lab' working hours (i.e. when pPCI not available). In-hospital TL was considered ORT only in *remote* patients who self-presented to hospitals without a cath lab or *central* patients who self-present out of 'cath lab' hours. Patient who were deemed ineligible for either TL or pPCI were still deemed to have received ORT for the purposes of this study. (e.g. ORT might represent no RT if the patient presented late)

For the purposes of this study patient pathways were created after consultation with several local experts and refined through multiple iterative stages - based on location of presentation (ambulance or self-presentation), initial management (PHT, in-hospital TL or PCI), reperfusion outcome and subsequent management. A new pathway was added where required after reviewing patients' clinical letters. This led to the identification of 13 distinct pathways in total.

The reasons for lack of ORT were determined from the notes review, they were recorded and described using descriptive statistics. Where the reason for lack of ORT was not explicitly recorded in the notes then the case was reviewed by a local subject expert (cardiologist) to determine the cause of lack of ORT. These were then characterised, quantified and reported using descriptive statistics

Data analysis and statistics

The data set for continuous data was presented as mean ± standard deviation (SD), while categorical data were presented as an absolute value, percentage or both. The Chi-square test was used for comparison of the relationship between remote vs. central location patients in terms of LV function and whether or not ORT was received. A p-value of <0.05 was considered statistically significant. All tests were performed using Microsoft Office Excel 2007.

Ethics

The study was approved by the ethical review panel of the School of Pharmacy and Life Sciences at Robert Gordon University. Caldecott approval was obtained from NHS Highland.

Results

During the study period, 627 patients were coded for acute MI, after applying the inclusion and exclusion criteria 131 STEMI patients were identified (Figure 1). Of the 131 STEMI patients, 83 (63%) were male (age 64 ± 13 years) and 48 (37%) were female (age 72 ± 11 years). Thirteen distinct clinical pathways were identified (Table 1). Eighty two (62%) patients were classed as *central* and 49 (38%) were *remote* (Table 2).

Place of definitive treatment

The majority of patients, 102 (78%) were treated at some point in their journey at the regional centre, some patients, 3 (2%) were treated at the rural hospital only while 26 (20%) were admitted out of working hours, did not reperfuse after TL and were transferred to the tertiary centre bypassing the regional centre.

Reperfusion therapy (RT)

Of the 131 STEMI patients, 26 (20%) received pPCI, 73 (56%) received TL and 32 (24%) received no RT. Of the 73 patients that received TL, reperfusion occurred in 48 (66%) and among those, 41 (85%) received convalescent PCI. The 25 (19%) that did not clinically reperfuse were treated with either rescue PCI, 21 (84%) or conservatively 4 (16%) (3 had convalescent PCI and one had no further therapy). Of the 32 patients that received no initial RT, 24 (75%) received convalescent PCI. (Table 1)

Optimal Reperfusion Therapy (ORT)

In total, 71 (54%) patients received ORT. Of the 52 patients receiving in-hospital TL 3 (6%) were self-presenters, while an additional 9 (17%) were not eligible for PHT and thus considered to have received ORT. Of the 34 patients who received no-RT, 12 (35%) patients were not suitable for TL and 2 (6%) had reperfused by the time of first medical contact.

Influence of time of day and remoteness

Central patients were more likely to receive ORT than *remote* patients (53 (65%) vs. 20 (41%); Chi-square = 7.05, DF =130, $p < 0.01$). The influence of location and time of presentation on the initial treatment of remote and central patients are shown in Figure 2 comparing working hours (a) and out of working hours (b)

Left ventricular (LV) function

Of the 131 patients, 33 (25%) had a normal LV function, 43 (33%) had a mild LV dysfunction, 29 (22%) were moderate, and 14 (11%) severe. The majority of patients who had a normal / mild LV (dys)function after STEMI were from the PHT group n (79%), while in the pPCI group n (58%) had a normal LV function (Figure 4). There was no difference between *central* and *remote* patients in terms of normal/mild LV impairment (45 (62%) vs. 31 (53%); p=0.35) although the study was under powered to show differences.

Barriers to ORT

Each of the 60 cases where ORT was not delivered was discussed with a cardiologist and the reason for 'no ORT' identified. These included include 38 (63%) cases where PHT was not given (due to lack of trained staff), 4 (7%) cases where poor inter-hospital communication led to no RT and 9 (15%) cases where the patients presented late. In 7 (12%) cases there was either a non-diagnostic ECG or atypical symptoms.

Discussion

This is the first paper to report differences between *remote* and *central* patients in an area which employs a hybrid reperfusion approach to STEMI care (both pPCI and TL used). The results show a clear variation in care between *remote* and *central* patients. What was not expected was the lower proportion of patients who received no-RT during office hours at the regional centre compared with all other periods. While there was no obvious difference in clinical outcomes measured by significant LV dysfunction between the *remote* and *central* groups the numbers are too small to be able to draw any definitive conclusions about any potential harm.

Results from this study are generally comparable with the Euro Heart Survey Acute Coronary Syndromes (EHS-ACS)[19] and the Global Registry of Acute Coronary Events (GRACE)[20]. In both studies, the majority of patients were male with a mean age similar to that in this present study. Interestingly, more *central* patients in our study received pPCI than in the EHS-ACS study, although these data are older and according to a more recent national audit of PCI, 91% of patients located within 90 minutes of a PCI centre were treated with pPCI[21]. This percentage is significantly higher than our *central* pPCI patients which can be explained by in-hours only availability of the 'cath lab'.

pPCI is the gold standard treatment for STEMI and has been shown to have mortality advantages over thrombolysis in several trials[6,22]. However, the majority of trials showing superiority of pPCI have compared pPCI with hospital not pre-hospital TL although equivalence has been shown more recently with pre-hospital TL, presumably the earlier the TL is given, the more likely it is to be effective. In our study, the proportion of STEMI patients who received pPCI was heavily influenced by the cath lab opening hours (limited to office hours) therefore the majority of STEMI patients

did not receive pPCI. There was obviously a major difference between *remote* and *central* patients in this regard with no remote patients receiving pPCI.

Thrombolysis as a treatment for STEMI was established in the 1980s after the ISIS trials using streptokinase[23] and until the emergence of pPCI was the mainstay of reperfusion treatment. It is well recognised that TL is most effective when given early (e.g. within 1 hr of artery occlusion). In the real world setting this is rarely achievable due to several factors including delayed call for help and sometimes limited availability of pre-hospital staff to deliver TL. This is a particular issue in remote areas in the UK where there is a relative lack of trained paramedics and thus remote patients are potentially at a double disadvantage being too far from a cath lab and served by ambulance staff with a lower chance of having paramedic crew. Our data reflect this reality with fewer patients in remote areas receiving PHT.

Despite the differences noted in the use of pPCI and TL there were no obvious difference in outcomes and indeed LV function was, if anything, more often normal in the TL subgroup, although the numbers were small making firm conclusions more difficult. There were only a small number of deaths in our cohort and it is therefore difficult to draw conclusions about mortality. Prior studies have reported higher mortality in remote MI patients[24]. The reasons for this are unknown but likely to be multifactorial. Due to the small numbers in many studies of remote and rural patients involved it is difficult to draw firm conclusions although one study suggested the increased mortality rates for remote acute MI patients did not appear to be related to lower quality of care[25]. A simple explanation to the higher mortality rates could be due to an older population that resides in remote areas, while studies suggest that variation in STEMI treatment could be attributed to the fact that patients with advanced age and co-morbidities, are less likely to be treated with RT despite the data confirming that these patients would benefit significantly from such treatment[26,27]. However,

we did not include pre-hospital deaths in our cohort and therefore are unsure what the over all death rate from acute MI is.

This current study also quantified the barriers to ORT. Four barriers were identified including: poor communication between hospitals; late presentation; non-diagnostic ECGs or atypical symptoms. However, the most frequent barrier encountered was the lack of PHT administered by paramedics most commonly due to a lack of a paramedic on the crews. Paramedics are experts in pre-hospital care and play a vital role in PHT administration. A study to test paramedic's ability to identify patients eligible for thrombolytic therapy, and thus reducing call-to-needle time, concluded that a mean potential saving time of 41 minutes is achieved[28]. Service providers need to take this into consideration. In this study's sample, the majority of non-ORT patients were eligible for PHT if trained paramedics were in place – this demonstrates a health inequality in remote areas with regard to STEMI patients getting access to ORT. Our area therefore needs to ensure that all PHT responders are trained to provide appropriate treatment to individual patients and to ensure that all ambulances are staffed with paramedics. This is not an insurmountable issue and with better staff training pre-hospital thrombolysis (PHT) administered by trained paramedics or dual response primary care physician / general practitioner (GP) could likely be increased. Training primary care physicians in remote areas showed significant reduction in delay from call to needle time, by an average of 17 minutes. Diagnosis made by the GP was reliable and safe with 95% of the initial STEMI diagnosis being confirmed[29]. In our area we provide a telemetric and decision support service from the coronary care unit but clearly our result show that more work is needed to increase us of PHT in *remote* patients.

Delayed call for help is a well identified barrier to ORT which was outside the scope of this study due to poor and inconsistent documentation of this parameter. The GRACE registry of 11,543 patients with acute coronary syndrome indicated that the median time between symptoms onset and call for help was 139 minutes, suggesting even with the

most advanced systems of care some barriers are difficult to overcome[20]. The reason could be that published guidelines attempting to standardise STEMI care are not individualized for each facility, thus adherence to STEMI guidelines might not be feasible in remote sites. According to the study of Bata et al., ORT can be achieved through rapid pre-hospital diagnosis and improving systems of care[30]. However, little effort has been made in identifying the causes of such challenges in remote areas and this is an area for future research.

Although transfer distance has a major impact on ischaemic time[31], and PHT is the optimal therapy if door-to-balloon ≥ 90 min[11,12], PHT was not utilised for most remote patients, and a higher use of PHT was seen in central patients with considerable variations between working and out of working hours. Holmes et al. reported that a successful regional care model can reduce the disparity of care between off-hours and working hours for patients with STEMI[32]. Therefore establishing a local policy to provide consistent quality of care might be key factor in providing ORT.

Limitations

This study has limitations, firstly, the retrospective design depends on the quality of routinely collected data and certain parameters such as time from symptom onset to call for help were not consistently available. Nevertheless, we were able to include all STEMI and due to the national radiology reporting system and electronic patient discharge letters were able to report clinical data for all patients. Secondly, the use of Google maps[18] to measure travel time via a car is not a validated tool for an ambulance and paramedic crews might be quicker due to their training, road use and advanced driving skills. Furthermore, volume of traffic at different times of the day or year will affect travel times. Notwithstanding this limitation, Google maps provided a systematic approach. A further limitation was that while we had data on hospital of first admission and home address we could not always confirm that myocardial infarction had occurred at the home address and it is possible a small number of patients had their

event elsewhere although if there had been a large different in location this would have been obvious from a disconnect between home location and local hospital which was not found. Finally, the study sample included patients diagnosed with STEMI and admitted to a hospital. Any patient, who did not survive a STEMI before being admitted was therefore not included. This may affect interpretation of the data and conceal mortality differences but addressing this limitation was outside the scope of the study.

Conclusion

This study has shown that ORT delivery is suboptimal in the whole study region; furthermore, a clear difference in access to ORT exists between *central* and *remote* patients demonstrating a health inequality between patients living in *central* and *remote* areas. Disappointingly, *remote* patients, while geographically unable to reach an available 'cath lab' in time, were also less likely to receive PHT and therefore potentially exposed to higher risk. Reassuringly during working hours, the vast majority of central patients received pPCI which reflects ORT, but more needs to be done to improve PHT use out of hours. This study confirms that communication and pathways could be improved (e.g. bypassing non-PCI capable hospitals) but the major barrier identified to the delivery of ORT was the lack of trained paramedics which should be addressed with some urgency.

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Table and Figure Legends

Table 1: Reperfusion therapy pathway

pPCI (primary percutaneous coronary intervention), PHT (pre-hospital thrombolysis)

Table 2: Drive times

Figure 1: CONSORT diagram of study recruitment

Figure 2: Central vs. remote a) cath lab open b) cath lab closed

Figure 4: Proportion of patients with normal LV function stratified by initial reperfusion therapy.

Table 1 Reperfusion therapy pathways (n=131)

Prehospital thrombolysis (PHT), primary Percutaneous Coronary Intervention (pPCI)

Pathway	Thrombolysis location	Outcome from thrombolysis	PCI type	Patients n (%)
1	None	N/A	pPCI	26 (20)
2	PHT	Reperfused	Convalescent	8 (6)
3	PHT	Reperfused	None	3(2)
4	PHT	Not Reperfused	Rescue	6 (5)
5	PHT	Not Reperfused	Convalescent	2 (2)
6	PHT	Not Reperfused	None	0 (0)
7	Hospital	Reperfused	Convalescent	35 (27)
8	Hospital	Reperfused	None	3 (2)
9	Hospital	Not Reperfused	Rescue	12(9)
10	Hospital	Not Reperfused	Convalescent	1 (1)
11	Hospital	Not Reperfused	None	1 (1)
12	None	N/A	Convalescent	26 (20)
13	None	N/A	None	8 (6)

549 Table 2 **Patient distance from regional centre based on drive time**
550

Driving times (mins)	**Patients n (%)**
≤ 30	49 (37.0)
30-60	25 (19.0)
60-90	8 (6.0)
90-120	10 (8.0)
≥ 120	39 (30.0)

551

552 **Figure 1 CONSORT flow diagram**

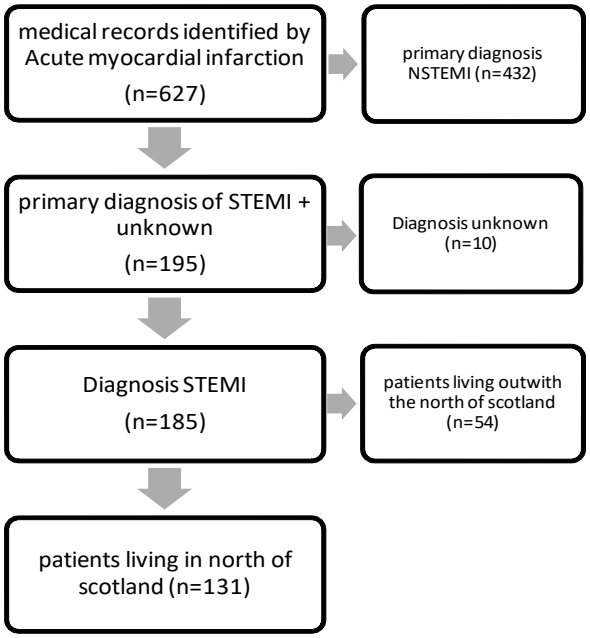

Figure 2a Initial reperfusion therapy when cath lab at regional centre closed

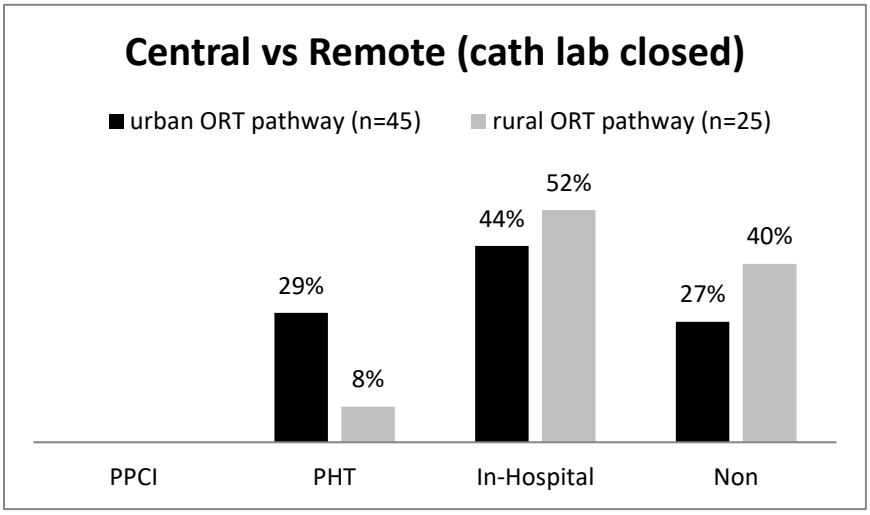

Figure 2b Initial reperfusion therapy when cath lab at regional centre open

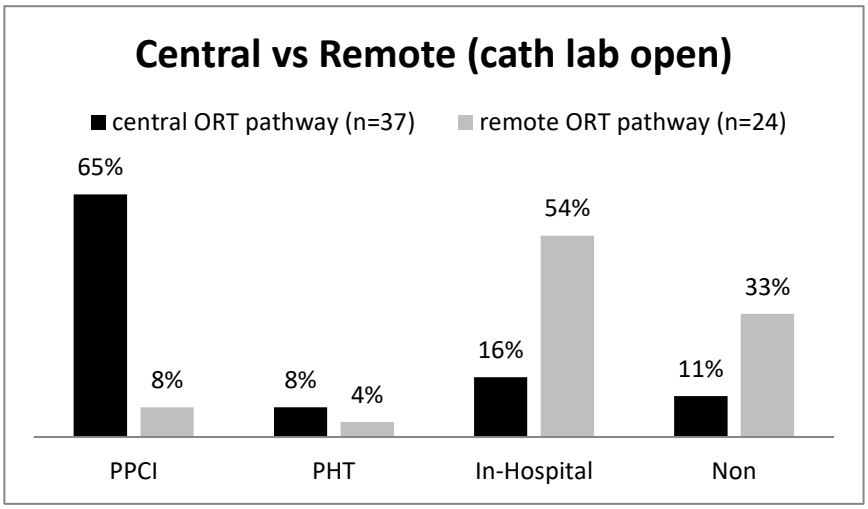

Figure 3 Percentage of patients with normal or mildly impaired LV function post myocardial infarction by initial reperfusion therapy. (Primary percutaneous coronary intervention (PPCI), prehospital thrombolysis (PHT).