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Review

Right ventricular myocardial infarction and adverse events from nitrates: A narrative review

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Abstract

Introduction
There is ubiquitous belief that right ventricular myocardial infarction (RVMI) patients are pre-load dependent, and that administering nitrates to this cohort may cause adverse events – most notably hypotension. This article charts a narrative history of RVMI and nitrates: from the initial recognition of RVMI and early support of the use of nitrates, through the spread of the view against nitrates, and to the recent publication of evidence once again supporting their use.

Methods
Four databases were systematically searched (PubMed, Embase, Medline, Web of Science) and results screened by title, then abstract, and finally full text. Results were presented using a chronological narrative structure.

Results
The view against the use of nitrates during RVMI can be traced back to a single 1989 cohort study of 28 patients, then later being adopted by a series of influential secondary evidence papers, and ultimately by international guidelines. In 2016, 2017 and 2019, new cohort studies totalling 1046 patients were presented, all of which concluded that nitrates are safe to administer during RVMI.

Conclusion
This article charts how a single retrospective cohort study with low statistical power came to form the dominant narrative on best practice despite complex and conflicting primary evidence.

Keywords:
myocardial infarction; nitroglycerin; right ventricle

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Introduction

There is ubiquitous belief that right ventricular myocardial infarction (RVMI) patients are pre-load dependent, and that administering nitrates to this cohort may cause adverse events – most notably hypotension (1-3). This view can be traced back to a single 1989 cohort study of 28 patients, then later being adopted by a series of influential secondary evidence papers, and ultimately by international guidelines (4). New cohort studies totalling 1046 patients were published in 2016, 2017 and 2019, all of which concluded that nitrates were safest when given for RVMI (5-7). This article aims to chart the history of RVMI and nitrates: from the initial recognition of RVMI and early support of the use of nitrates, through the spread of the view against nitrates, and the recent publication of evidence once again supporting their use.

Methods

As supported by the Joanna Briggs Institute, a three-part search strategy was used (8). First, an initial search of PubMed and Embase was undertaken using the keywords 'myocardial infarction', 'nitrate', 'inferior', 'right ventricular' and 'hypotension'. Relevant articles were then scanned for additional keywords, which were incorporated into a full systematic search on 20 January 2020. Due to delays related to the COVID-19 pandemic, the search was re-performed on 24 November 2020 on PubMed (Ovid, 1946-search date), Embase (Ovid, 1947-search date), Medline Complete (EBSCO, 1879-search date) and Web of Science Core Collection (Clarivate, 1900-search date). Limiters were used for English language. No date limitation was applied. Results were imported into Mendeley 2019 version 1.19.4 (Mendeley Ltd, London, UK), duplicates were removed and results filtered by Richardson-Tench et al's method of screening the title, then abstract, then full text (9). Finally, the reference lists of relevant articles were checked, and appropriate studies incorporated. Papers were assessed for inclusion by a single researcher, with the sole inclusion criteria of discussion surrounding adverse events (or their absence) following nitrate administration to RVMI. Exclusion criteria were articles that did not present primary evidence, administration of inhaled nitric oxide (as this does not cause systemic adverse events) and diagnosis of vasospasm (as nitrates often form definitive treatment for this cohort).

Results

The first stage search strategy of PubMed and Embase used to determine alternate keywords is shown in Tables 1 and 2.

There were five duplicates between the two lists, leaving 18 articles in total. The titles, abstracts and index terms of these 18 articles were reviewed to produce alternative search terms used for the full systematic search. The full systematic search results are shown in Tables 3 to 6.

Following the search, 628 citations were identified and uploaded to Mendeley 2019 (version 1.19.4). With duplications removed, 495 citations remained. First, these were screened by title, abstract and then full text by a sole reviewer for assessment against the inclusion criteria for the review. Second, the remaining 27 articles had their full text imported. Third, the reference list of the 27 studies selected for critical appraisal were screened, and seven additional potentially relevant studies added for critique. Of these 34 studies, seven present primary evidence discussing adverse events from nitrate administration during RVMI. The systematic search is summarised in Figure 1.

Table 1. Initial search of PubMed to determine keywords

Search	Query	Records retrieved
#1	"myocardial infarction"	240,620
#2	nitrate*	75,687
#3	"right ventric*"	61,101
#4	hypotension	344,109
#5	#1 AND #2 AND #3 AND #4	13
Limited to English language results		11

Table 2. Initial search of Embase to determine keywords

Search	Query	Records retrieved
#1	"myocardial infarction"	294,460
#2	nitrate*	114,889
#3	"right ventric*"	117,916
#4	hypotension	170,775
#5	#1 AND #2 AND #3 AND #4	12
Limited to English language results		12

Table 3. PubMed search results

Search	Query	Records retrieved
#1	"myocardial infarction" OR AMI OR infarct* OR "acute coronary syndrome*" OR ACS OR "heart attack" OR ischaem* OR ischem* OR STEMI OR NSTEMI OR "ST-elevation" OR "ST elevation" OR STEACS OR NSTEACS OR OMI	687,177
#2	nitrate* OR nitroglycerin OR trinitr* OR GTN OR TNG	95,963
#3	("right ventric*" OR RVMI OR RVEF OR V4R) OR (inferior OR IWMI)	188,205
#4	"adverse event" OR AE OR hypotension OR dysrhythmia OR arrhythmia OR bradycardia OR tachycardia OR disassociation OR block OR syncope OR arrest OR death OR mortality OR morbidity	6,025,635
#5	#1 AND #2 AND #3 AND #4	101
Limited to English language results		101

Table 4. Embase search results

Search	Query	Records retrieved
#1	myocardial infarction OR AMI OR infarct* OR acute coronary syndrome* OR ACS OR heart attack OR ischem* OR ischaem* OR STEMI OR NSTEMI OR ST#elevation OR STEACS OR NSTEACS OR OMI	1,262,230
#2	nitrate* OR nitroglycerin OR trinitr* OR GTN OR TNG	172,725
#3	(right ventric* OR RVMI OR RVEF OR V4R) OR (inferior OR IWMI)	356,643
#4	adverse event OR AE OR hypotension OR dysrhythmia OR arrhythmia OR bradycardia OR tachycardia OR disassociation OR block OR syncope OR arrest OR death OR mortality OR morbidity	4,914,935
#5	#1 AND #2 AND #3 AND #4	504
Limited to English language results		450

Table 5. Medline search results

Search	Query	Records retrieved
#1	"myocardial infarction" OR AMI OR infarct* OR "acute coronary syndrome*" OR ACS OR "heart attack" OR isch?em* OR ?STEMI OR "ST#elevation" OR ?STEACS OR OMI	449,713
#2	nitrate* OR nitroglycerin OR trinitr* OR GTN OR TNG	100,720
#3	("right ventric*" OR RVMI OR RVEF OR V4R) OR (inferior OR IWMI)	210,149
#4	"adverse event" OR AE OR hypotension OR dysrhythmia OR arrhythmia OR bradycardia OR tachycardia OR disassociation OR block OR syncope OR arrest OR death OR mortality OR morbidity	2,874,105
#5	#1 AND #2 AND #3 AND #4	58
Limited to English language results		44

Table 6. Web of Science search results

Search	Query	Records retrieved
#1	"myocardial infarction" OR AMI OR infarct* OR "acute coronary syndrome*" OR ACS OR "heart attack" OR isch$em* OR STEMI OR NSTEMI OR "ST?elevation" OR STEACS OR NSTEACS OR OMI	844,071
#2	nitrate* OR nitroglycerin OR trinitr* OR GTN OR TNG	240,155
#3	("right ventric*" OR RVMI OR RVEF OR V4R) OR (inferior OR IWMI)	213,088
#4	"adverse event" OR AE OR hypotension OR dysrhythmia OR arrhythmia OR bradycardia OR tachycardia OR disassociation OR block OR syncope OR arrest OR death OR mortality OR morbidity	3,378,283
#5	#1 AND #2 AND #3 AND #4	42
Limited to English language results		33

Discussion

1932 to 1974: First clinical description

Right ventricular myocardial infarction has been described in autopsy studies since at least 1932, but due to studies during the 1940s and 1950s was believed to have little haemodynamic impact (10-13). A 1943 study concluded that inducing severe RVMI in dogs produced no haemodynamic compromise; this was subsequently supported by a 1952 study (also of induced infarction in dogs) which went as far as to conclude "a normal, contractile right ventricular wall is not necessary for the maintenance of a normal circulation" (12,13). Further studies in 1952 and 1959 instead attributed any haemodynamic effects noted during RVMI to concomitant left ventricular failure (14,15). RVMI only received mainstream recognition as a unique clinical and haemodynamic syndrome following a cohort study of six patients by Cohn et al in 1974 (16). In this study, all six presented with hypotension in the 70–90 mmHg systolic range and jugular venous distention. Four additionally had clear lungs on imaging. During their time in hospital, all six were catheterised and found to have increased right atrial pressure (mean 20.2 mmHg – compared to a normal pressure of ~7–10 mmHg) with normal left ventricular end diastolic pressure, suggesting no meaningful left ventricular infarction (16,17). ECG showed five had inferior wall infarction (the sixth

was anterolateral), and four had third-degree blocks attributed to atrioventricular nodal ischaemia. Shock in three patients was effectively treated with volume loading. Two of these patients died in hospital, and autopsy confirmed right ventricular necrosis without other gross pathologies. The third shocked patient was administered a nitroprusside infusion that "increased cardiac output" and survived. The other three patients survived to discharge and were diagnosed based on similar clinical and ECG presentation.

The 1974 study by Cohn et al is a landmark paper for three reasons. First, it is the earliest published diagnosis of RVMI on living patients, and recognition of RVMI syndrome. Second, the triad of hypotension, jugular venous distention and clear lungs would form the basis of published discussion for the clinical presentation of RVMI in the following years and remains in use (with additions) today (18-22). Finally, it suggested fluid challenge was appropriate as first line therapy for hypotension, a view affirmed by subsequent studies and that also remains current today (19,23). Additionally, it stated "the ability of the right ventricle to maintain adequate left ventricular filling is impaired", reiterating the earlier theory that RVMI patients are at risk of low cardiac output (16,24,25). This paper is also notable as the first administration of nitrates to RVMI, with a beneficial outcome noted. Using the crude metric of citation count, this paper has had a significant impact on the literature, with over 700 citations at the time of writing.

1970s to 1980s: Ongoing research into clinical presentation

The 1974 paper by Cohn et al was the first in a series of papers over the following decade to investigate the clinical presentation of RVMI. Seven months later, Rotman et al presented a single case study of a patient death from RVMI, again stating the presence of hypotension, jugular venous distention, clear lung fields and inferior ST elevation (20). In 1979, Lorell et al presented a retrospective cohort study of 12 patients diagnosed with RVMI (21). All 12 had jugular venous distention with clear lungs, and nine presented with hypotension and increased right filling pressures. In 1981, Lloyd et al undertook a retrospective cohort study investigating the haemodynamics of 19 RVMI patients. Of the 19 patients, 13 were hypotensive and six experienced cardiogenic shock (22). These papers solidified Cohn et al's diagnostic triad and raised awareness of increased right atrial loading pressure due to decreased right ventricular output.

Further research also supported the hypothesis that fluid challenge was effective in offsetting any hypotension (21,22,26). In 1983, Goldstein et al performed a prospective interventional cohort study on seven dogs, inducing RVMI via right coronary artery balloon embolus, then testing the efficacy of fluid bolus (23). Fluids were found to be effective on all parameters; after

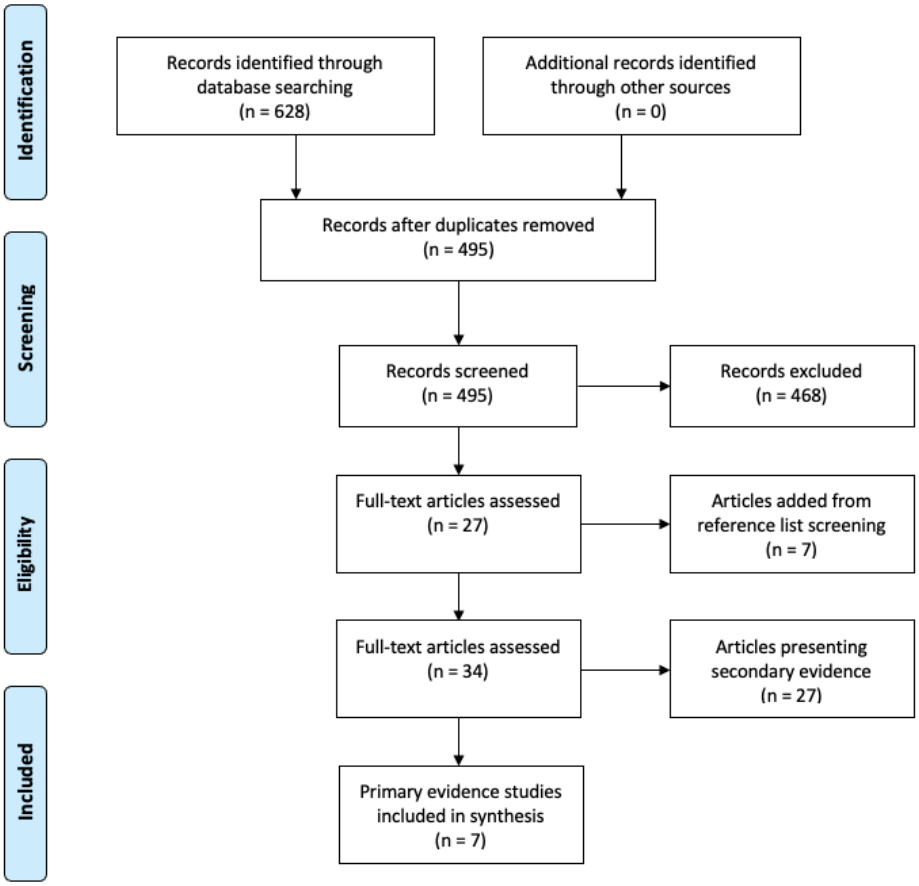

Figure 1. PRISMA diagram of the systematic search.

embolisation, cardiac output dropped from 1.9 L/m to 1.3 L/m in 5 minutes and increased to 1.8 L/m following a 500 mL fluid challenge over 10 minutes.

1989: First original research directly on nitrate safety during RVMI

Adverse events from nitrate administration during RVMI had been incidentally mentioned in seven papers in the decade following Cohn et al (22,27-32). Three (seven patients) had found evidence of transient hypotension, while four (35 patients) had not. All of these articles focussed on different topics, and overall the reliability of the evidence is poor. However, they would have little impact on the literature and all would be overshadowed by a far more influential study directly investigating the topic.

In 1989, Ferguson et al published the first primary evidence directly focussing on the effect of nitrates on the haemodynamics of patients experiencing inferior and right ventricular infarcts (4). Via a retrospective cohort study of two separate but overlapping populations, Ferguson et al tested two questions: does hypotension in response to nitrates predict RVMI (40 patients enrolled); and do RVMI patients have a higher rate of hypotension in response to nitrates (28 patients enrolled)? In the second research question tested, all 28 patients were experiencing dual inferior and RVMI (diagnoses based on ECG and enzymes) and administered nitrates. Of these, 20 (71%) developed hypotension (defined as a drop in systolic blood pressure over 30 mmHg) after nitrate administration. Another five developed hypotension spontaneously. This paper provides the first caution against nitrate administration during RVMI, stating "the administration of nitrates in patients with documented RV infarction may provoke a hypotensive response… patients with RV infarction may be exquisitely sensitive to changes in preload" (4).

However, the study contains several methodological weaknesses. Both the authors and later commentary acknowledge the sample size of 28 is small, and that they were retrospectively selected. Additionally, the authors acknowledge that their ECG interpretation technique was not reliable, as the method they used may not pick up all RVMIs when there is concomitant left ventricular infarction – such that only large RVMIs are detected. This means it is possible there are subtle RVMIs that weren't included in the RVMI arm of the study, potentially skewing the results towards a higher significance level. The authors ultimately concluded "the risks of nitrate administration in patients with known RV infarction awaits larger, prospective, randomised studies" (4). However, while every subsequent cohort study would conclude that nitrates may be safely be administered during RVMI, this evidence would be largely ignored. Ferguson et al's study would go on to instead form the dominant narrative and be cited over 50 times in the following 30 years – including by the American Heart Association in its inaugural 1996 guidelines, and by many of the significant studies on this topic that would later come (33).

1989 – 2016: The perspective against nitrates for right ventricular infarction

Interestingly, before Ferguson et al in 1989 the literature was partially supportive of the administration of nitrates to RVMI. The initial paper by Cohn et al stated that vasodilators could reduce left atrial filling pressure, in turn increasing right ventricular ejection fraction and finding that administration corrected shock (22). Dell'Italia et al and Hiroe et al concluded that there were no complications from nitroprusside and nitroglycerin infusions respectively (29,31). Contrasting evidence was also presented instead suggesting increased rates of hypotension: Sharpe et al presented a case study mentioning transient hypotension from sublingual nitroglycerin, while Flaherty et al found the same from nitroglycerin infusion in four patients (27,30). Raabe and Chester concluded nitrate infusions were safe; however, their patients were simultaneously administered saline infusions, and interrogation of the underlying data is suggestive that hypotension may have been likely without this volume support (28). Therefore, until this point the evidence was strongly suggestive of the need for large-scale, prospective investigation.

However, this would not occur, and following the publication of Ferguson et al in 1989, the recommendation against providing nitrates in the setting of inferior or right infarcts became widespread, and sometimes misunderstood – for example, a 1990 case study takes the data from the first cohort in Ferguson et al, and erroneously applies it to the research question in the second cohort (34). Evidence contradicting Ferguson et al's findings would fail to achieve similar recognition: in 1994, Mittal et al published a follow-up to their 1992 study, cumulatively investigating 13 RVMI patients and concluding "we therefore feel that the cautious use of small doses of nitrates and diuretics under close monitoring is safe. This is contradictory to widely held views" (35,36). This work would seldom be cited. By contrast, that same year (1994) the most widely cited study since Cohn et al originally described clinical RVMI would be published. Kinch and Ryan published their influential paper 'Right ventricular infarction' in the New England Journal of Medicine, an article that provides a major summary of all research to date and recommendations for practice (37). Importantly, the paper endorses avoiding nitrates due to the risk of severe hypotension, with this recommendation based off Ferguson et al, Lloyd et al (which conversely concluded nitrates were beneficial during RVMI) and Goldstein et al's 1983 study (no nitrates are administered in this study). This paper has since been cited over 500 times – including by the American Heart Association guidelines in 1996 (33).

This view against administering nitrates during RVMI soon became pervasive. In 1999, an expert opinion article by Funk and McGuire studied the risk of adverse events from nitrates and, despite concluding adverse events appear to occur in less than 5% of cases, concluded that "because of their dependence on preload, patients suspected of having RVMI should be given nitrates with great caution, if at all" (38). This article cited Ferguson et al and Kinch and Ryan (itself reliant on Ferguson

et al) in reaching this conclusion. In 2002, Goldstein provided a guideline on the management of right ventricular ischaemia (39). Goldstein's paper draws attention to the importance of maintaining pre-load and recommends avoiding nitrates for RVMI, again with Ferguson et al the only evidence cited. This article has since been cited over 280 times. A 2003 randomised cohort study on right ventricular mortality rates by Jacobs et al advocated for avoiding nitrates in RVMI (40). The 2010 American Heart Association guidelines again recommended avoiding nitrates for RVMI, as did another 2013 expert opinion paper by Ondrus et al (41,42). All of these papers are solely reliant on the single 28-patient cohort study by Ferguson et al, with no discussion of the limitations of the primary data or mention of the 14 other articles published before 2010 presenting relevant data. As this popular opinion grew, further research on the topic diminished: during the two decades from Mittal et al until the next cohort study in 2016, the totality of evidence is limited to six case studies – four suggesting an increased risk of hypotension, and two suggesting nitrates are equally safe during RVMI (43-48).

2016 – present: New cohort evidence is presented

In 2016, Robichaud et al published a retrospective cohort study of 805 participants comparing the rate of adverse events (including hypotension defined both as a systolic <90 mmHg and as a drop of over one-third) when glyceryl trinitrate (dose 400 mcg) was administered to inferior and other region infarctions (5). The paper conducted a subgroup analysis on RVMI (based on ECG criteria) compared to inferior-only infarction and stated: "we did not find an association between hypotension after NTG administration and the previously described standard 12-lead ECG features suggestive of right ventricular involvement in inferior STEMI" (p.5). The study also found no statistically significant difference between adverse events when glyceryl trinitrate was administered to inferior and other region infarcts (8.9% to 8.3%, p-value 0.80). However, the study is limited by no information being provided on the number of RVMI patients, investigation of isolated RVMI, and by using a more lenient definition of hypotension (systolic <90 mmHg instead of the more standard <100 mmHg). However, the article also contains two unique strengths. First, patients with multi-region infarcts were included in the inferior group, meaning analysis it is more likely to return a result that inferior rates of adverse events are highly; this essentially skews the study away from the conclusion that inferior and non-inferior acute myocardial infarctions are equally safe when administered nitrates, making that conclusion more reliable. Second, both computer and physician ECG interpretation were performed, with no significant differences found.

The overall hypotension rate was 8.2%, suggesting that hypotension will occur in one in every 12 patients who are administered glyceryl trinitrate, and that this will be regardless of the region where the infarction is occurring. The paper concluded "although it is widely recommended in the medical literature to use caution when administering nitroglycerin to patients with inferior STEMI, the only study supporting this statement is a retrospective cohort study published in 1989 by Ferguson et al" (5).

In 2017, McConnell et al published an abstract of a retrospective cohort study (presented at a conference) that compared the risk of adverse events between inferior and right ventricular infarctions administered nitrates in the pre-hospital environment (6). This paper included broader definitions of adverse events, including bradycardia <60 bpm, hypotension <100 mmHg systolic, hypotension drop >1/3, GCS drop 2+, syncope, arrest and death. The study included 46 patients, with 19 in the RVMI arm and 27 in the inferior-only arm. The rates of adverse events were 57.9% (n=11) to 37% (n=10) respectively, producing a p-value of 0.2. Arrest or death occurred in neither group. Due to the statistical insignificance of findings, the authors concluded that the "results of this study suggest no difference in the rate of AEs between patients with inferior STEMI and STEMI with RVI when NTG is administered in the prehospital setting" (6).

In 2019, Bosson et al conducted a prospective observational cohort study of 195 patients comparing the rates of adverse events (including bradycardia, hypotension as a systolic <100 mmHg, hypotension as a drop of >30 mmHg, and arrest) based on which vessel was occluded on angiography (7). Their study found a relative risk of hypotension to right coronary artery occlusions of 0.64 (95% CI: 0.21-1.95) and the relative risk of bradycardia to right coronary artery occlusions of 1.30 (95% CI: 0.57-2.94), both statistically insignificant. However, this study only stated the vessel where the lesion occurred and did not confirm the infarct territory; variations in cardiac artery anatomy mean a site of lesion in some circumstances cannot be assumed to affect a particular myocardial region (19). Bosson et al distinguished between right coronary artery and other vessel lesions, and while right coronary artery occlusion is the primary cause of right ventricular infarction, it is also caused by ischaemia to the marginal branches of the left anterior descending in 15% of cases (7,29,30,37). Additionally, the study measured hypotension at emergency department arrival and afterwards; with an average pre-hospital transport time of 11 minutes, it is possible that transient hypotension occurred with paramedics and was not included in study data. This may have skewed data towards a finding that nitrates are safe. The authors acknowledge this and justify it by reference to the clinical unimportance of brief hypotension that doesn't persist over the 11-minute average transport time, and by stating that this study reflects the clinical realities of treatment rather than laboratory conditions. The study concluded that giving nitrates to right coronary artery occlusions was the safest of any lesion site.

Limitations

This article does not seek to suggest that the current orthodoxy against nitrate administration during RVMI should be overturned. Instead, it suggests that the evidentiary picture is more nuanced than currently appreciated, and that evaluation of the totality of evidence should occur to judge the reliability of current

guidelines.

Conclusion

The belief that nitrates should be withheld for right ventricular and inferior myocardial infarctions is now so ubiquitous that is included in the European Journal of Cardiology guidelines, American Heart Association guidelines, and multiple expert commentary pieces both domestic and international. Importantly, none of these current articles evaluate the original underlying data. Of the cohort studies of primary evidence, the three cohort studies published from 2016 to present, cumulatively including 1046 patients, found nitrates could be administered without increased risk, while the 1989 cohort study of 28 patients remains the only cohort evidence suggesting increased risk. A quantitative review is appropriate to determining best practice.

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Competing interests

The author declares no competing interests. The author of this paper has completed the ICMJE conflict of interest statement. This article may partially contribute towards a postgraduate thesis.

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References

1. Lavonas EJ, Drennan IR, Gabrielli A, et al. Part 10: special circumstances of resuscitation. 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation 2015;132:S501-18.
2. Ibanez B, James S, Agewall S, et al. 2017 ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur Heart J 2018;39:119-77. Available at: https://academic.oup.com/eurheartj/article/39/2/119/4095042
3. Thomsett R, Cullen L. The assessment and management of chest pain in primary care: a focus on acute coronary syndrome. Aust J Gen Pract 2018;47:246-51.
4. Ferguson JJ, Diver DJ, Boldt M, Pasternak RC. Significance of nitroglycerin-induced hypotension with inferior wall acute myocardial infarction. Am J Cardiol 1989;64:311-4.
5. Robichaud L, Ross D, Proulx MH, et al. Prehospital nitroglycerin safety in inferior st elevation myocardial infarction. Prehosp Emerg Care 2016;20:76-81.
6. McConnell AH, Davis M, Van Aarsen K, Columbus M, Lewell M. LO33: Prehospital adverse events associated with nitroglycerin use in STEMI patients with right ventricle infarction. CJEM 2017;19(S1):S39. Available at: www.cambridge.org/core/product/identifier/S1481803517000951/type/journal_article
7. Bosson N, Isakson B, Morgan JA, et al. Safety and effectiveness of field nitroglycerin in patients with suspected ST elevation myocardial infarction. Prehosp Emerg Care 2019;23:603-11. Available at: https://doi.org/10.1080/10903127.2018.1558318
8. Joanna Briggs Institute. JBI Manual for Evidence Synthesis [Internet]. Aromataris E, Munn Z, editors. JBI; 2020. Available at: https://wiki.joannabriggs.org/display/MANUAL/11.2.5+Search+Strategy [Accessed 14 February 2020].
9. Richardson-Tench M, Nicholson P, Taylor BJ, Kermode S, Roberts KL. Research in nursing, midwifery and allied health: evidence for best practice. 6th edn. South Melbourne, Australia: Cengage Learning Australia; 2018.
10. Lisa JR, Ring A. Myocardial infarction or gross necrosis: analysis of one hundred necropsies. Arch Intern Med 1932;50:131-41. Available at: http://archinte.jamanetwork.com/article.aspx?doi=10.1001/archinte.1932.00150140138008
11. Appelbaum E, Nicolson GHB. Occlusive diseases of the coronary arteries. Am Heart J 1935;10:662-80. Available at: https://linkinghub.elsevier.com/retrieve/pii/S0002870335902599
12. Starr I, Jeffers WA, Meade RH. The absence of conspicuous increments of venous pressure after severe damage to the right ventricle of the dog, with a discussion of the relation between clinical congestive failure and heart disease. ibid. 1943;26:291-301. Available at: https://linkinghub.elsevier.com/retrieve/pii/S0002870343903254
13. Kagan A. Dynamic responses of the right ventricle following extensive damage by cauterization. Circulation 1952;5:81623. Available at: www.ahajournals.org/doi/10.1161/01.CIR.5.6.816
14. Zaus EA, Kearns WM. Massive infarction of the right ventricle and atrium. ibid. 1952;6:593-8. Available at: www.ahajournals.org/doi/10.1161/01.CIR.6.4.593
15. Wade WG. The pathogenesis of infarction of the right ventricle. Heart 1959;21:545-54. Available at: http://heart.bmj.com/cgi/doi/10.1136/hrt.21.4.545
16. Cohn JN, Guiha NH, Broder MI, Limas CJ. Right ventricular infarction: clinical and hemodynamic features. Am J Cardiol 1974;33:209-14.
17. Magder S. Right atrial pressure in the critically ill. Chest 2017;151:908-16. Available at: https://linkinghub.elsevier.com/retrieve/pii/S0012369216622833
18. Levin T, Goldstein JA. Right ventricular myocardial infarction. Saperia G, editor. Waltham (MA): UpToDate; 2019.
19. Albulushi A, Giannopoulos A, Kafkas N, et al. Acute right ventricular myocardial infarction. Expert Rev Cardiovasc Ther

2018;16:455-64. Available at: https://doi.org/10.1080/14779072.2018.1489234
20. Rotman M, Norman BR, Hawley J. Right ventricular infarction: a haemodynamic diagnosis. Heart 1974;36:941-4.
21. Lorell B, Leinbach RC, Pohost GM, et al. Right ventricular infarction. Clinical diagnosis and differentiation from cardiac tamponade and pericardial constriction. Am J Cardiol 1979;43:465-71.
22. Lloyd EA, Gersh BJ, Kennelly BM. Hemodynamic spectrum of "dominant" right ventricular infarction in 19 patients. ibid. 1981;48:1016-22.
23. Goldstein JA, Vlahakes GJ, Verrier ED, et al. Volume loading improves low cardiac output in experimental right ventricular infarction. J Am Coll Cardiol 1983;2:270-8. Available at: http://dx.doi.org/10.1016/S0735-1097(83)80163-6
24. Fishberg A. Heart Failure. 2nd edn. Philadelphia, USA: Lea & Febiger; 1940.
25. Harrison TR. Failure of the circulation. New York, USA: Williams & Wilkins; 1939.
26. Carter T, Ellis K. Right ventricular infarction. Crit Care Nurse 2005;25:52-62. Available at: https://doi.org/10.4037/ccn2005.25.2.52
27. Sharpe DN, Botvinick EH, Shames DM, et al. The noninvasive diagnosis of right ventricular infarction. Circulation 1978;57:483-90. Available at: www.ahajournals.org/doi/10.1161/01.CIR.57.3.483
28. Raabe DS, Chester AC. Right Ventricular Infarction. Chest 1978;73:96-9. Available at: https://linkinghub.elsevier.com/retrieve/pii/S0012369216612552
29. Hiroe M, Sekiguchi M, Hirosawa K, Shibata J. Hemodynamic assessment in the medical treatment of acute myocardial infarction: The effects of various vasodilators and catecholamines. Jpn Circ J 1981;45:591-622. Available at: www.mendeley.com/research/geology-volcanic-history-eruptive-style-yakedake-volcano-group-central-japan/
30. Flaherty JT, Becker LC, Bulkley BH, et al. A randomized prospective trial of intravenous nitroglycerin in patients with acute myocardial infarction. Circulation 1983;68:576-88. Available at: www.ahajournals.org/doi/10.1161/01.CIR.68.3.576
31. Dell'Italia LJ, Starling MR, Blumhardt R, Lasher JC, O'Rourke RA. Comparative effects of volume loading, dobutamine, and nitroprusside in patients with predominant right ventricular infarction. ibid. 1985;72:1327-35. Available at: www.ahajournals.org/doi/10.1161/01.CIR.72.6.1327
32. Jugdutt BI, Warnica JW. Intravenous nitroglycerin therapy to limit myocardial infarct size, expansion, and complications: effect of timing, dosage, and infarct location. Circulation 1988;78:906-19.
33. Ryan TJ, Anderson JL, Antman EM, et al. ACC/AHA guidelines for the management of patients with acute myocardial infarction. J Am Coll Cardiol 1996;28:1328-419. Available at: https://linkinghub.elsevier.com/retrieve/pii/S0735109796003920
34. Brandes W, Santiago T, Limacher M. Nitroglycerin-induced hypotension, bradycardia, and asystole: report of a case and review of the literature. Clin Cardiol 1990;13:741-4. Available at: http://doi.wiley.com/10.1002/clc.4960131015
35. Mittal SR. Isolated right ventricular infarction. Int J Cardiol 1994;46:53-60. Available at: https://linkinghub.elsevier.com/retrieve/pii/0167527394901171
36. Mittal SR, Pamecha S, Rohatgi R, Saxena R, Gokhroo R. Isolated right ventricular infarction. ibid. 1992;36:187-96. Available at: https://linkinghub.elsevier.com/retrieve/pii/016752739290006O
37. Kinch JW, Ryan TJ. Right ventricular infarction. N Engl J Med 1994;330:1211-7.
38. Funk D, McGuire TJ. Nitroglycerin in the out-of-hospital treatment of chest pain. Prehosp Emerg Care 1999;3:266-8.
39. Goldstein JA. Pathophysiology and management of right heart ischemia. J Am Coll Cardiol 2002;40:841-53. Available at: http://dx.doi.org/10.1016/S0735-1097(02)02048-X
40. Jacobs AK, Leopold JA, Bates E, et al. Cardiogenic shock caused by right ventricular infarction: a report from the SHOCK registry. ibid. 2003;41:1273-9. Available at: http://dx.doi.org/10.1016/S0735-1097(03)00120-7
41. O'Connor RE, Brady W, Brooks SC, et al. Part 10: acute coronary syndromes. 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation 2010;122(S3).
42. Ondrus T, Kanovsky J, Novotny T, et al. Right ventricular myocardial infarction: from pathophysiology to prognosis. Exp Clin Cardiol 2013;18:27-30.
43. Nallamothu BK, Saint M, Saint S, Mukherjee D. Double Jeopardy. N Engl J Med 2005;353:75-80. Available at: www.nejm.org/doi/10.1056/NEJMcps050117
44. Moye S, Carney MF, Holstege C, Mattu A, Brady WJ. The electrocardiogram in right ventricular myocardial infarction. Am J Emerg Med 2005;23:793-9.
45. Smith SW, Heegaard W, Bachour FA, Brady WJ. Acute myocardial infarction with left bundle-branch block: disproportional anterior ST elevation due to right ventricular myocardial infarction in the presence of left bundle-branch block. ibid. 2008;26:342-7.
46. Muhammad KI, Kapadia SR. Anterior ST-segment elevation with right coronary artery occlusion: A unique case of isolated right ventricular infarction. Angiology 2008;59:622-4.
47. Parekh P, Agrawal N, Vasavada A. Isolated RV myocardial infarction presenting with systemic hypertension minimally responsive to nitroglycerin. Case Reports 2014;8;2014 Available at: https://casereports.bmj.com/lookup/doi/10.1136/bcr-2014-204494
48. Peters A, Lakhter V, Bashir R. Under-pressure: Right Ventricular Infarction. Am J Med 2015;128:966-9. Available at: http://dx.doi.org/10.1016/j.amjmed.2015.05.007
49. Cabin HS, Clubb KS, Wackers FJT, Zaret BL. Right ventricular myocardial infarction with anterior wall left ventricular infarction: An autopsy study. Am Heart J 1987;113:16-23. Available at: https://linkinghub.elsevier.com/retrieve/pii/0002870387900044
50. Ratliff NB, Hackel DB. Combined right and left ventricular infarction: Pathogenesis and clinicopathologic correlations. Am J Cardiol 1980;45:217-21.