International Journal of Cardiology Cardiovascular Risk and Prevention 19 (2023) 200215

Contents lists available at ScienceDirect

International Journal of Cardiology Cardiovascular Risk and Prevention

journal homepage: www.journals.elsevier.com/international-journal-of-cardiology-cardiovascular-risk-and-prevention

Occult myocardial injury is prevalent amongst elderly patients in the hospital-at-home setting. A retrospective analysis of 213 patients

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ARTICLE INFO

Handling Editor: D Levy

Keywords:
Myocardial injury
Hospital-at-home
Telemedicine
Troponin
Occult myocardial damage

ABSTRACT

Background: Hospital-at-Home (HAH) is a valid alternative for in-hospital stay for a wide variety of clinical indications. Occult myocardial injury, associated with acute illness, mainly occurs in patients with a background of non-obstructive coronary disease. The aim of this study was to describe the prevalence of this phenomenon in our HAH population.

Methods: A retrospective description and analysis of data collected for patients admitted to the Sheba beyond's HAH services during 14 months.

Results: During a period of 14 months (7/10/21–6/12/22), blood troponin measurements were available for 213 patients (median age 78 years, 52% males) hospitalized mainly for infectious causes. The median HS (highly sensitive) troponin level was 7.7 ng/L (IQR = 13.2 ng/L) (the normal upper limit is 12 ng/L) with 31% of all patients demonstrating an abnormally increased troponin level (68/213). Of all patients, 64% had a background diagnosis of a cardiovascular disease (138/213), of whom, 49% had abnormal HS troponin levels (68/138). No patient suffered from acute cardiac function deterioration and no patient died during their hospital-at-home stay.

Conclusion: The prevalence of occult myocardial injury amongst elderly patients admitted to hospital-at-home stay for diagnoses other than myocardial infarction is relatively high but it is not associated with worse short-term clinical outcomes.

1. Introduction

Home hospitalization is currently a well-established alternative for in-hospital stay in a wide variety of clinical indications. Previous publications present the satisfactory outcomes in the Hospital-at-Home (HAH) setting [1,2]. Currently, approved and widely accepted indications for HAH include several infectious diseases such as mild to moderate COVID-19 infection, other viral and bacterial pneumonia, urinary tract infections and cellulitis. Patients suffering from exacerbations of chronic diseases including Chronic Obstructive Pulmonary Disease (COPD) and Congestive Heart Failure (CHF) are also considered eligible for HAH [3–5]. Accepted contraindications for this setting include patients with respiratory insufficiency and those with hemodynamic instability. Myocardial damage is generally accepted as a contraindication for patients' monitoring and treatment at home. Nevertheless, COVID-19 patients, that were the first patients' population to be treated, worldwide, in the HAH settings, demonstrated a large proportion of myocardial injury and involvement [6].

Myocardial damage which is not associated with acute coronary obstruction, appearing most often during a non-cardiovascular disease, is also known as Type II Acute Myocardial Infarction (AMI) [7]. It is more common amongst elderly patients and is associated with a relatively high one-year mortality and higher incidence of 30-days major cardiovascular events [8,9] compared to those without evidence of myocardial injury. Causes of Type II AMI include various stress-states such as sepsis, accounting for at least 19% of cases [9]. Amongst several other risk factors, high blood troponin measurements are defining, the risk of Type 2 AMI patients for worse clinical outcomes

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https://doi.org/10.1016/j.ijcrp.2023.200215
Received 14 August 2023; Received in revised form 10 September 2023; Accepted 17 September 2023

[10].

In Sheba Beyond we established a HAH service utilized for acute-care patients with the intention to support and serve as an alternative for in-hospital stay of acutely ill patients, suffering from the aforementioned, widely accepted HAH indications. We have already published previous case reports regarding the safety and feasibility of this model [11]. During home-hospitalizations of complicated patients we collected various physiologic parameters, amongst others, patients' troponin blood levels. These measurements are not routine during in-hospital stay but are part of our efforts for thickening their safety measures during their stay at home. The aim of this study was to describe the prevalence of occult myocardial damage amongst these patients, representing Type II AMI.

2. Methods

2.1. Patients' selection and troponin tests

Patients' data were collected from the electronic medical records (EMR) of patients admitted to Sheba-Beyond HAH service between October 2021 and December 2022. Patients aged 18 and above, who underwent at least one blood troponin measurement during their home hospitalization, met the inclusion criteria for this study. Our exclusion criteria included patients with type 1 AMI (S-T elevation MI) but no such patients appeared during the study period.

Troponin is routinely measured for each patient upon admission, and during further laboratory follow-up, based on clinical requirements. Venous blood samples were drawn by certified nurses and transported from each patient's residence to the laboratory in a cold, temperature-insulating container. For determining a normal troponin result, we used the Sheba medical center's HS (highly sensitive) troponin I kit parameters [Beckman Coulter (Access hsTnI (High Sensitivity Troponin I Assay) 3rd Generation)], in which troponin values of 0–12 ng/L are considered within the normal range. All patients went through routine, 12-lead electrocardiography in order to exclude type 1 acute myocardial infarction (e.g., ST – segment elevation). Occult myocardial damage was defined as positive/elevated HS troponin levels without clinical correlates (such as angina pectoris) and/or electrocardiographic evidence of acute myocardial ischemia.

2.2. Statistical analysis

Normally distributed continuous variables are reported as the mean ± SD (standard deviation), while continuous variables with markedly skewed distributions are reported as the median and interquartile range (IQR, 25th to 75th percentile). The Shapiro–Wilk test was used to test for normality. For statistical analyses, the statistical software 'R' was used. For measuring the linear relationship between continuous variables, we used Pearson's correlation coefficient. Patients' records were addressed after an institutional review board approved patients' data analysis (Institutional Review Board approval # 8828-21-SMC).

3. Results

During a period of 14 months (7/10/21–6/12/22), 213 eligible patients who were admitted to the Sheba-Beyond's HAH service was included in the study. The median age was 78 years (IQR = 19). 111 patients were females (52%). The most frequent hospitalization diagnosis was moderate to severe COVID-19.

The median troponin level was 7.7 ng/L (IQR = 13.2 ng/L). Overall, 31% of all patients admitted had an abnormal troponin result (68/213). 64% of all patients had a background diagnosis of a cardiovascular disease (138/213), of whom, 49% had abnormal troponin level (68/138). Most abnormal troponin values were recorded upon admission, during the first day of their HAH period. Patients' characteristics according to their blood troponin levels are presented in Table 1. Patients with pathologically elevated levels of troponin had significantly higher blood levels (median 37 ng/L (IQR = 55) vs. 5.3 ng/L (IQR = 4.1); $p < 0.0001$), they were older (median 86 vs. 74 years, $p < 0.01$), and had significantly higher frequency of cardiovascular disease on their background (86% vs. 54%; $p < 0.01$). Regression analysis presented in Fig. 1 show a statistically significant increase in the likelihood of positive troponin values as patients become older. The regression becomes more evident with increasing statistical significance in those patients with background cardiovascular morbidities. In the group of patients who had abnormal troponin level, there was no statistically significant relationship between age and troponin (p-value = 0.3299, Pearson coefficient 0.11). In the group who had normal troponin, there was a

Table 1
Patients' characteristics according to troponin levels.

Patients' characteristics	Normal Troponin (N = 145)	Abnormal Troponin (N = 68)	P value
Patients' demographics			
Age; years (median (IQR))	74 [12]	86 [13]	<0.01
Gender (% males)	44	56	0.13
Background diagnoses			
Cardiovascular (%)	54	86	<0.01
Hematological/ Malignant (%)	21	33	0.08
Neurological/Psychiatry (%)	13	19	0.3
Metabolic/Endocrine (%)	45	54	0.2
Autoimmune/ Inflammatory (%)	15	7	0.15
Respiratory (%)	14	11	0.6
Laboratory Parameters			
Troponin (ng/L) (median (IQR))	5.3 (4.1)	37 (55)	<0.0001
Positive COVID-19 PCR (%)	88	72	<0.01
Hospitalization Characteristics			
Length of Stay (days, median (IQR))	2 [2]	3 (2.25)	<0.01
Urgent referral to in-hospital stays	0	0	NA
Mortality (%)	0	0	NA

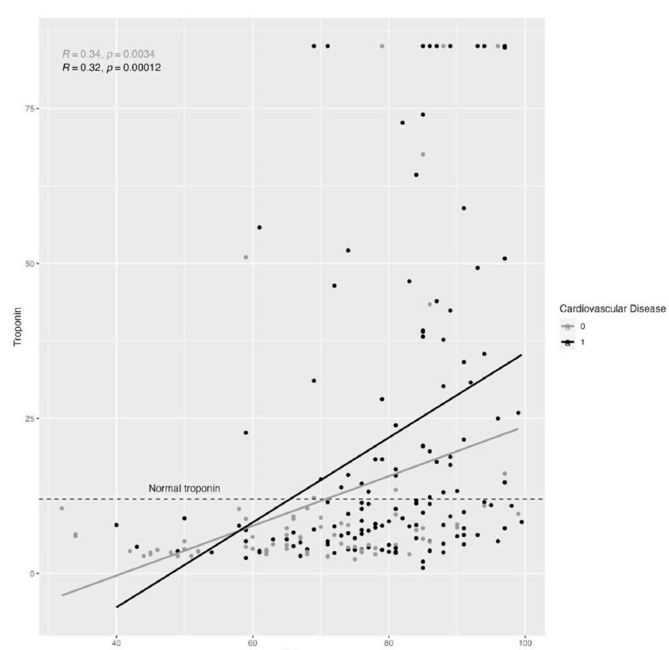

Fig. 1. Regression analysis for positive troponin and age, according to presence/absence of background cardiovascular morbidity.

statistically significant positive relationship between age and troponin level (p-value = 0.0003178, Pearson coefficient 0.29). Surprisingly, a larger percentage of patients with positive troponin levels had primary hospitalization diagnoses other than COVID-19 infection (with 88% vs. 72%; $p < 0.01$). The median length of hospitalization stay was one day longer for those with elevated troponin (3 days vs. 2; $p > 0.01$). No patient died during their HAH stay, regardless of their blood troponin levels.

4. Discussion

The global implementation of HAH alternative to in-hospital stays is essential. However, it should not occur until the safety of HAH settings is ensured. Objective assessment of clinical outcomes during and after HAH hospitalizations is critical. Additionally, when including more severely ill patients in HAH programs, it is crucial to consider potential options for deterioration. One such potential complication is occult myocardial damage, which can manifest during acute non-cardiovascular diseases. No previous study has addressed this important issue so far.

In the current study we show that occult myocardial injury, as indicated by increased blood concentration of troponin, performed by a highly sensitive kit [13–15], is indeed frequent in the HAH patients' population. As expected, we show that it is more frequent amongst elderly patients and even more so amongst elderly patients with chronic, cardiovascular morbidities in their background. Surprisingly, non-COVID-19 patients had more frequent myocardial damage, in contrast to previously published data relating to a high prevalence of myocardial injury in this group of patients [16,17]. This could be partially explained by the fact that the clinical presentation and aggressiveness of COVID-19 serotypes during this study duration tended to be more subtle.

Diagnosis of occult myocardial damage during HAH stay is important both in the short- and in the long-term management of patients: in the long-term, it is established that type 2 AMI patients bare higher risk for subsequent acute coronary obstruction and may benefit from further, coronary-risk stratification after recovering from their acute illness [18,19]. Furthermore, these patients are at increased risk for non-cardiovascular re-hospitalizations [20]. Therefore, this group of patients should be referred, upon discharge from HAH stay for further cardiovascular workup. In the short-term, it is established that these patients have a higher risk for cardiovascular mortality and increased risk for MACE (Major Cardiovascular Events) during their hospitalization and shortly after discharge [19]. These patients' risk for MACE and mortality would be aggravated by concurrent electrolyte disturbances [12] (e.g., hypokalemia that bares increased risk for arrythmia during myocardial ischemia [21,22]) and pending arrythmias (e.g., prolongation of QTc (QT-corrected) [23], predisposing to potentially catastrophic ventricular arrythmias. These insights should impose actions on behalf of HAH services organizations: troponin levels should be monitored and accordingly, with respect to the service capacity and capabilities, should be referred to the in-hospital setting or monitored for electrolyte disturbances and/or cardiac conduction anomalies during their hospital stay. In an upcoming publication by our group, we describe the high frequency of electrolyte disturbances amongst HAH patients' population and the quest to validate 6-lead ECG applications that would enable frequent, self-ECG monitoring by patients at their homes.

5. Conclusion

In the current study we found a significant prevalence of occult myocardial damage amongst patients admitted to the HAH service, even when their primary hospitalization diagnoses are non-cardiovascular. In light of the above, we emphasize the importance of routine troponin measurements in this population. As HAH environment is globally advocated, incorporating this practice to the HAH routine is crucial, potentially helping to identify patients at higher risk of clinical deterioration. For elderly patients with background cardiovascular diagnoses the recommendation for troponin follow-up becomes essential. Also, we recommend that whenever clinically appropriate, post-discharge coronary investigations should be included in the follow-up of these patients.

6. Limitations

This was a single-center study and the milieu of patients was homogenous, according to our inclusion criteria for HAH eligibility. Therefore, larger, multi-center studies, that will sample larger and heterogenous patients' populations are warranted.

Credit author statement

MY, AE, BG, SG: Conceptualization, AE, SA, GE, BA, KLR, HH: Data curation, MY, SG, BG: Formal analysis, NA: Funding acquisition, MY, AE, SA, GE, BA, KLR, BG, HH, SG: Investigation, MY, AE, SA, GE, BA, KLR, BG, HH, SG: Methodology, MY, SG: Project administration, GB, GS: Resources, MY, AE: Software, GS; KLR: Supervision, MY, AE, SA, GE, BA, KLR, BG, HH, SG: Validation, MY, AE, SA, GE, BA, KLR, BG, HH, SG: Visualization, MY, AE, SA, GE, BA, KLR, BG, HH, SG: Roles/Writing – original draf, MY, AE, SA, GE, BA, KLR, BG, HH, SG: Writing – review & editing.

References

[1] A. Hecimovic, V. Matijasevic, S.A. Frost, Characteristics and outcomes of patients receiving hospital at home services in the south west of sydney, BMC Health Serv. Res. 20 (1) (2020) 1–5. Dec 1, https://bmchealthservres.biomedcentral.com/articles/10.1186/s12913-020-05941-9. (Accessed 5 March 2023).

[2] S.Q. Ko, J. Goh, Y.K. Tay, N. Nashi, B.M.Y. Hooi, N. Luo, et al., Treating acutely ill patients at home: data from Singapore, Ann. Acad. Med. Singapore 51 (7) (2022 Jul 1), 392–9, https://pubmed.ncbi.nlm.nih.gov/35906938/. (Accessed 5 March 2023).

[3] Hospital-at-Home | AHA. https://www.aha.org/hospitalathome. (Accessed 15 July 2023).

[4] Why HaH. https://www.hospitalathome.org.uk/what-is-hospital-at-home. (Accessed 15 July 2023).

[5] D.M. Levine, K. Ouchi, B. Blanchfield, K. Diamond, A. Licurse, C.T. Pu, et al., Hospital-level care at home for acutely ill adults: a pilot randomized controlled trial, J. Gen. Intern. Med. 33 (5) (2018 May 1) 729. /pmc/articles/PMC5910347/. (Accessed 15 July 2023).

[6] Çakmak Karaaslan Ö, M.O. Özilhan, O. Maden, O. Tüfekçioğlu, Prevalence of cardiac involvement in home-based recovered coronavirus disease 2019 (COVID-19) patients: a retrospective observational study, Ir. J. Med. Sci. 191 (5) (2022 Oct 1), 2057–62, https://pubmed.ncbi.nlm.nih.gov/34714493/. (Accessed 15 July 2023).

[7] N.R. Smilowitz, P. Subramanyam, E. Gianos, H.R. Reynolds, B. Shah, S.P. Sedlis, Treatment and outcomes of type 2 myocardial infarction and myocardial injury compared to type 1 myocardial infarction, Coron. Artery Dis. 29 (1) (2018) 46, pmc/articles/PMC5722665/. (Accessed 15 July 2023).

[8] N. Furie, A. Israel, L. Gilad, G. Neuman, F. Assad, I. Ben-Zvi, et al., Type 2 myocardial infarction in general medical wards: clinical features, treatment, and prognosis in comparison with type 1 myocardial infarction, Medicine (United States) 98 (41) (2019 Oct 1). https://journals.lww.com/md-journal/Fulltext/2019/10110/Type_2_myocardial_infarction_in_general_medical.18.aspx. (Accessed 5 March 2023).

[9] S. Gupta, S.R. Vaidya, S. Arora, A. Bahekar, S.R. Devarapally, Type 2 versus type 1 myocardial infarction: a comparison of clinical characteristics and outcomes with a meta-analysis of observational studies, Cardiovasc. Diagn. Ther. 7 (4) (2017 Aug 1), 34858–34358, https://cdt.amegroups.com/article/view/14605/html. (Accessed 5 March 2023).

[10] C. Taggart, K. Monterrubio-Gómez, A. Roos, J. Boeddinghaus, D.M. Kimenai, E. Kadesjo, et al., Improving risk stratification for patients with type 2 myocardial infarction, J. Am. Coll. Cardiol. 81 (2) (2023 Jan 17), 156–68, https://pubmed.ncbi.nlm.nih.gov/36631210/. (Accessed 5 March 2023).

[11] G. Barkai, H. Amir, O. Dulberg, E. Itelman, G. Gez, T. Carmon, et al., "Staying at Home": a pivotal trial of telemedicine-based internal medicine hospitalization at a nursing home, Digit Health 8 (2022). https://pubmed.ncbi.nlm.nih.gov/36133002/. (Accessed 5 March 2023).

[12] A. Shiyovich, H. Gilutz, Y. Plakht, Serum electrolyte/metabolite abnormalities among patients with acute myocardial infarction: comparison between patients with and without diabetes mellitus, Postgrad 133 (4) (2021) 395–403. https://pubmed.ncbi.nlm.nih.gov/33275496/. (Accessed 29 July 2023).

[13] J.A. De Lemos, C.R. Defilippi, Prevalence and significance of detectable troponins as measured by highly sensitive assays in the general population, Coron. Artery Dis. 24 (8) (2013 Dec) 705–709.

[14] M. Reiter, R. Twerenbold, T. Reichlin, P. Haaf, F. Peter, J. Meissner, et al., Early diagnosis of acute myocardial infarction in the elderly using more sensitive cardiac troponin assays, Eur. Heart J. 32 (11) (2011 Jun) 1379–1389.

[15] F.R. Kalaji, S. Albitar, Predictive value of cardiac troponin T and I in hemodialysis patients, Saudi J Kidney Dis Transpl 23 (5) (2012) 939–945.

[16] K.S. Bhatia, H.P. Sritharan, J. Chia, J. Ciofani, D. Nour, K. Chui, et al., Cardiac complications in patients hospitalised with COVID-19 in Australia, Heart Lung Circ. 30 (12) (2021 Dec 1) 1834–1840.

[17] H.P. Sritharan, K.S. Bhatia, W. van Gaal, L. Kritharides, C.K. Chow, R. Bhindi, Association between pre-existing cardiovascular disease, mortality and cardiovascular outcomes in hospitalised patients with COVID-19, Front Cardiovasc Med 10 (2023). https://pubmed.ncbi.nlm.nih.gov/37476577/. (Accessed 29 July 2023).

[18] A.P. DeFilippis, A.R. Chapman, N.L. Mills, J.A. De Lemos, A. Arbab-Zadeh, L. K. Newby, et al., Assessment and treatment of patients with type 2 myocardial infarction and acute nonischemic myocardial injury, Circulation 140 (20) (2019 Nov 12), 1661–78, https://www.ahajournals.org/doi/abs/10.1161/CIRCULATIONAHA.119.040631. (Accessed 29 July 2023).

[19] K.M. Eggers, T. Baron, A. Gard, B. Lindahl, Clinical and prognostic implications of high-sensitivity cardiac troponin T concentrations in type 2 non-ST elevation myocardial infarction, Int J Cardiol Heart Vasc 39 (2022 Apr 1). https://pubmed.ncbi.nlm.nih.gov/35198728/. (Accessed 29 July 2023).

[20] S. Rocheleau, J. Eng-Frost, K. Lambrakis, E. Khan, B. Chiang, N. Wattchow, et al., Twelve-month outcomes of patients with myocardial injury not Due to type-1 myocardial infarction, Heart Lung 31 (Supplement 3) (2023) S237. https://pubmed.ncbi.nlm.nih.gov/37225600/. (Accessed 29 July 2023).

[21] L. Sun, B. Han, Y. Wang, W. Zhu, J. Jiang, A. Zou, et al., A new scoring system for predicting ventricular arrhythmia risk in patients with acute myocardial infarction, Clin. Interv. Aging 18 (2023) 283–292.

[22] L. Sun, L. Mao, A. Zou, B. Chi, X. Chen, Y. Ji, et al., [Development and validation of a clinical predictive model for the risk of malignant ventricular arrhythmia during hospitalization in patients with acute myocardial infarction], Zhonghua Wei Zhong Bing Ji Jiu Yi Xue 33 (4) (2021 Apr 1), 438–42, https://pubmed.ncbi.nlm.nih.gov/34053487/. (Accessed 29 July 2023).

[23] K.E. Sandau, M. Funk, A. Auerbach, G.W. Barsness, K. Blum, M. Cvach, et al., Update to practice standards for electrocardiographic monitoring in hospital settings: a scientific statement from the American Heart association, Nov 7, Circulation 136 (19) (2017). E273–344, https://www.ahajournals.org/doi/abs/10.1161/CIR.0000000000000527. (Accessed 29 July 2023).