Iran J Nucl Med. 2024;32(2):165-174 [Serial No. 63]

Homepage: https://irjnm.tums.ac.ir/

ORIGINAL RESEARCH ARTICLE

Negligible influence of proton pump inhibitors on gastric wall uptake of [^{99m}Tc]Tc-MIBI in myocardial perfusion imaging

Raheleh Hedayati[1], Seyedeh Farnaz Siadati[2], Nahid Yaghoobi[2], Hadi Malek[2], Zahra Jamshidi Araghi[2], Mohammad Chehreghani[2], Leila Hassanzadeh[2,3]

[1]Department of Nuclear Medicine, School of Medicine, Hasheminejad Hospital, Iran University of Medical Sciences, Tehran, Iran

[2]Department of Nuclear Medicine, School of Medicine, Rajaie Cardiovascular, Medical and Research Center, Iran University of Medical Sciences, Tehran, Iran

[3]Department of Molecular Imaging, Faculty of Advanced Technologies in Medicine, Iran University of Medical Sciences, Tehran, Iran

ARTICLE INFO

Article History:
Received: 29 February 2024
Revised: 18 April 2024
Accepted: 21 April 2024
Published Online: 20 May 2024

Keyword:
Proton pump inhibitors
Gastric wall uptake
[^{99m}Tc]Tc-MIBI
Myocardial perfusion imaging
SPECT/CT

*Corresponding Author:
Dr. Leila Hassanzadeh
Address: Iran University of Medical Sciences, Shahid Hemmat Highway, 14496-14535, Tehran Iran.
Email: hassanzadeh.l@iums.ac.ir

ABSTRACT

Introduction: Myocardial perfusion imaging (MPI) faces a challenge in diagnostic accuracy due to gastric wall uptake (GWU). Previous studies have linked GWU to proton pump inhibitors (PPIs) intake, but only a minority of patients on PPIs show activity accumulation. Our study aimed to investigate the influence of PPIs on GWU in MPI by single photon emission computed tomography (SPECT) and assess the necessity or benefits of discontinuing PPIs before the procedure.

Methods: The 368 patients who underwent a two-day stress/rest [^{99m}Tc]Tc-MIBI SPECT/CT MPI were divided into three groups: (i) Control group (n=114, without the consumption of any gastroprotective medication), (ii) continued medication(n=48, on PPI treatment) and (iii) discontinued medication (n=206, PPI discontinued for one day or more before MPI). Rest SPECT images were analysed for clinically relevant GWU.

Results: Based on our study, out of 114 patients in group (i),16 individuals (14%), and 10 patients from 48 patients in group (ii) (20.8%) demonstrated radioactivity accumulation in the gastric wall. In group (iii), despite discontinuing PPIs use, 20.3% of patients showed GWU. Statistical analysis of these three groups and their subgroups did not show any significant difference in terms of gastric wall uptake of [^{99m}Tc]Tc-MIBI in MPI.

Conclusion: Concisely, our study found no significant link between PPI use and gastric wall activity in MPI. Further data is needed before adjusting drug guidelines in nuclear medicine centers. Multicenter studies with larger patient cohorts must explore the PPI-GWU relationship, utilizing SPECT/CT scans for precise interference location determination.

Use your device to scan and read the article online

How to cite this article: Hedayati R, Siadati SF, Yaghoobi N, Malek H, Jamshidi Araghi Z, Chehreghani M, Hassanzadeh L. Negligible influence of proton pump inhibitors on gastric wall uptake of [^{99m}Tc]Tc-MIBI in myocardial perfusion imaging. Iran J Nucl Med. 2024;32(2):165-174.

https://doi.org/10.22034/IRJNM.2024.129572.1617

INTRODUCTION

Technetium-99m methoxy isobutyl isonitrile ([99mTc]Tc-MIBI) is a lipophilic cation that, upon intravenous injection, moves passively across sarcolemmal and mitochondrial membranes driven by a substantial electronegative transmembrane potential gradient, facilitated by its lipophilic nature and positive charge. This positively charged lipophilic molecule is drawn towards the negatively charged mitochondria, where it becomes trapped and retained [1-3]. SPECT/CT imaging technique with [99mTc]Tc-MIBI in myocardial perfusion imaging is the most employed procedure for evaluating patients with suspected or diagnosed coronary artery disease (CAD) and assessing myocardial viability [4-6].

The presence of unintentionally absorbed radiopharmaceutical in infra-diaphragmatic organs such as the liver, gall bladder, bowel, and occasionally gastric lumen leads to the creation of artifacts during the interpretation of myocardial perfusion imaging (MPI) [7-9]. The presence of scattered radioactivity from sub-diaphragmatic organs can cause artifacts especially in the lower wall of the left ventricle. These artifacts can lead to reduced image quality and less-than-ideal interpretation in a significant portion of MPI studies [10, 11]. Consistent accurate interpretations are critical in scientific investigations. The radioactive uptake in the gastric, liver and intestines can sometimes superimpose on the heart, predominantly affecting the inferior segments. This overlap can cause photons to scatter from the abdominal area into the inferior region, artificially enhancing the perceived brightness of these segments. For instance, if the influence of abdominal activity is more pronounced in resting images than in stress images, this elevated brightness can simulate ischemia. Furthermore, increased abdominal radioactivity adjacent to the heart can paradoxically reduce the brightness of the impacted cardiac segment because of filtered back-projection. This effect can subtract counts from areas immediately neighboring a highly bright region because of ramp filtering. In severe instances, activity in the liver or intestines can completely mask a portion of the heart [10-13].

One of the sub-diaphragmatic regions that can absorb activity and cause artifacts is the stomach and gastric wall. The association between the absorption of [99mTc]Tc-MIBI in the gastric wall and the use of proton pump inhibitors (PPIs) has been discussed in previous studies[14-17]. Previous research on the topic of gastric wall uptake (GWU) is notably limited, often characterized by small sample sizes. In the study by Gholamrezanezhad et al., the only significant exploration on the subject, 1056 consecutive outpatients were described, with only 1.9% of patients showing gastric wall hyperactivity [18]. This low prevalence of GWU contrasts with the higher prevalence of 81% and 36% seen in studies by Goel et al. and Singh et al., respectively [19, 20]. There have been significant discrepancies in the reported studies regarding the percentage of PPIs consumers with GWU. Additionally, the possibility of using SPECT/CT images to diagnose of GWU more accurately from other abdominal regions, as well as the issues related to discontinuation of PPIs in our patients, prompted us to investigate the relationship between the use of these medications and the absorption of activity in the gastric wall. A prospective study was conducted to evaluate GWU in three groups of patients: (i) Control, not on any gastroprotection medication. (ii) Continued PPIs medication, and (iii) Discontinued PPIs with different intervals.

METHODS

Study population

Between April 2022 and July 2023, spanning a 15-month period, this prospective study was carried out at the Department of Nuclear Medicine in Rajaee Cardiovascular Medical and Research Center (CMRC). The study was granted formal approval by the Iran University of Medical Sciences Ethics Committee (IR.IUMS.FMD.REC.1400.481), and all participating patients provided written informed consent. In accordance with the department's policy, patients were instructed to discontinue the use of PPIs approximately one week prior to undergoing MPI imaging based on the current protocol, which is used in our center. Participants who voluntarily agreed to enroll in the study were categorized into one of three groups: (i) Control group, which did not take any gastroprotective medication, (ii) Continued PPIs group, consisting of patients who continued taking PPIs on the day of imaging, and (iii) Discontinued PPIs group, comprising patients who ceased taking PPIs prior to the day of imaging.

If activity was observed in the gastric cavity of patients but it was indeterminate whether the activity was in the gastric wall or solely in the cavity, these patients were excluded from the study. Final analysis incorporated a total of 368 patients. On the day designated for MPI, after obtaining pertinent clinical and cardiac histories, a comprehensive evaluation was carried out for

all enrolled patients. This evaluation involved administering a questionnaire encompassing demographic information, the utilization of gastroprotective medications (such as PPIs or Histamine-induced gastric acid secretion antagonist (H2A)), adherence to the medication regimen, and the duration of medication intake or discontinuation prior to the MPI procedure. A total of 368 patients were categorized into three study groups: (i) control group (n=114, 31%), consisting of patients not taking any gastroprotective medication (PPIs or H2A), (ii) continued PPIs group (n=48, 13.1%), comprising patients who maintained administration of PPIs for a minimum of 2 weeks, uninterrupted until the day of imaging, and (iii) discontinued PPIs group (n=206, 55.9%), consisting of patients who were regularly taking PPIs but discontinued their use for at least one day prior to the scheduled MPI imaging (Figure 1).

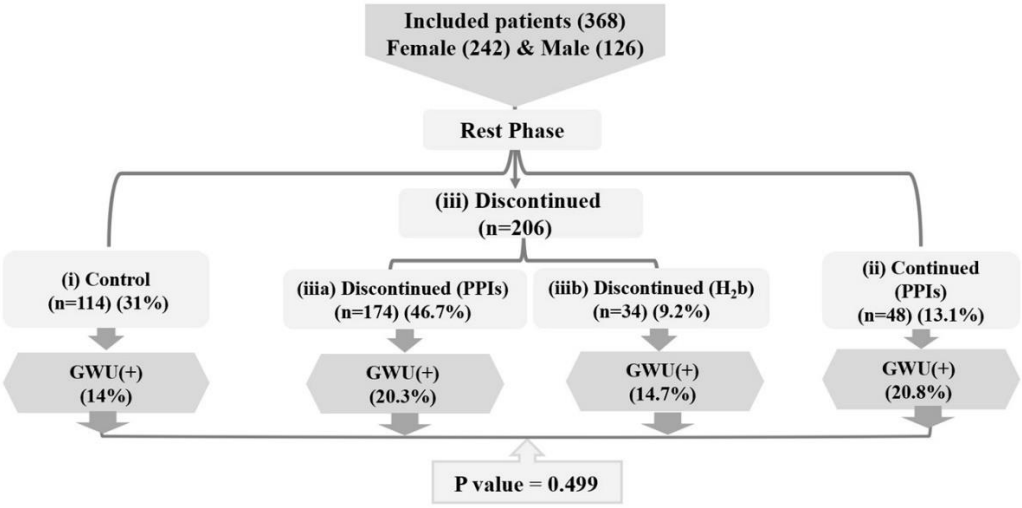

Figure 1. The flowchart depicts the procedure for patient enrolment, group allocation, and the analysis of eligible patients based on scores of 1, 2, or 3 for gastric wall uptake

Per the routine protocol at our center, patients were advised to stop their PPI medications one week before the scheduled imaging day. However, due to variations in adherence to these instructions, patients presented at the center with different discontinuation periods, ranging from a week to a day, and in certain instances, no medication discontinuation occurred. As a result, patients were classified into their respective groups based on these specific discontinuation periods.

Imaging protocol

All subjects underwent stress/rest myocardial perfusion imaging utilizing MIBI gated SPECT/CT, following a two-day protocol consistent with the guidelines established by the American Society of Nuclear Cardiology, which were strictly followed in our facility [21]. Patients were instructed to fast for 4 hours and abstain from caffeine or beta-blockers within 24 hours prior to the examination. The radiochemical purity of [^{99m}Tc]Tc-MIBI kits was evaluated, with purity exceeding 90% meeting USP-39 standards. The stress study utilized pharmacological agents (Dipyridamole, 56 mg/kg/minute for 6 minutes) or exercise (TMT; Bruce protocol). Patients received 444-518 MBq of MIBI at peak stress, adjusted for body weight. On the second day of imaging, the rest phase occurred, during which patients refrained from vigorous activity but did not fast. MIBI was intravenously administered at the stress phase dosage, followed by imaging 45 to 60 minutes later. A standard meal (200 mL of milk) was consumed post-injection to minimize extracardiac activity interference.

Data acquisition

The patients underwent imaging with a dual-head SPECT/CT gamma camera (Siemens Symbia system T16/T6/T2/T Series) 45 to 60 minutes after injection. The imaging parameters included a zoom of 1.64 cm, a matrix size of 128×128, 28 seconds per view, and 16 views. A low-energy all-purpose collimator was used with a detector configuration of 90, starting angle of 45 degrees, and a rotation of 90 degrees. The imaging was performed in a noncircular (auto) orbit and supine position, with arms positioned above the head for both stress and rest studies. Additionally, a low-dose CT scan was used for attenuation correction.

Data analysis

The MPI rest images of the patients were reviewed independently by two experienced

nuclear medicine physicians, blinded to both the patients' medical history and group assignments. Initially, the planar projection images were evaluated. If any areas of increased activity accumulation were observed, the subsequent step involved analyzing the SPECT/CT images to precisely determine the location of the activity accumulation. To ensure consistency in the imaging protocol, the decision was made to evaluate the rest phase images in this study, as they remain unchanged when compared to the two different stress phases (exercise or pharmacologic). In addition, considering the inconsistent findings regarding activity accumulation intensities in the rest and stress phases from previous studies [18, 22], and taking into account our center's observation of higher activity accumulation during the rest phase compared to the stress phase, we decided to focus on evaluating the rest phase in this study. The qualitative assessment of stomach wall activity was conducted on a scale of 0 (no activity) to 1 (activity less than that in the myocardium), 2 (activity almost equivalent to that in the myocardium), and 3 (activity greater than that in the myocardium) (Figure 2). Scores of 0 and 1 were considered clinically insignificant, reflecting minor interference in the assessment of myocardial perfusion. Scores of 2 and 3 were regarded as clinically relevant, potentially impacting the assessment of myocardial perfusion significantly. A third reader resolved any discrepancies.

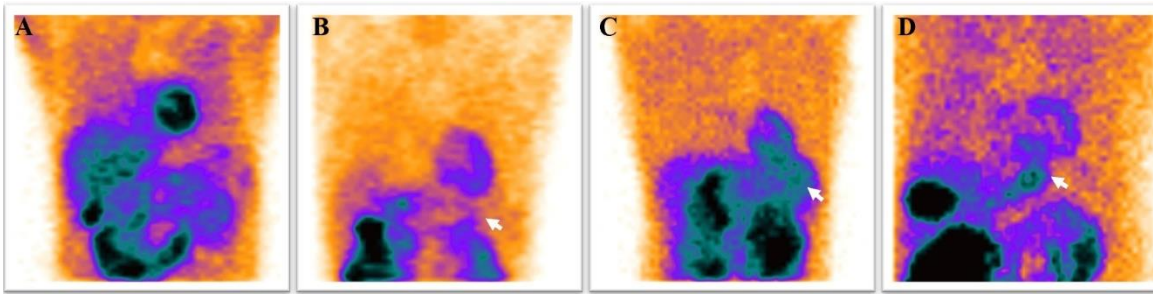

Figure 2. Evaluation of Stomach Wall Tracer Uptake (SWU) employing an ordinal scale from 0 to 3. Score 0 signifies the absence of stomach wall activity (**A**), Score 1 indicates faint tracer activity in the stomach wall, less than that in the myocardium (arrow) (**B**), Score 2 denotes moderate activity in the stomach wall, nearly equivalent to that in the myocardium (arrow) (**C**), and Score 3 represents intense tracer activity in the stomach wall, surpassing myocardial tracer activity (arrow) (**D**)

Statistical analysis

The statistical analyses were conducted utilizing SPSS version 27.0 for Windows, developed by SPSS Inc. in Chicago, IL, USA. Categorical and dependent variable was the presence of activity in the gastric wall (GWU) and was reported as numbers (percentages), whereas continuous variables like age and body mass index (BMI) were presented as mean ± standard deviation and those with non-normal distribution reported with median. Qualitative comparison between two groups was conducted using the chi-square test. In most analyses, the P-value was obtained from Pearson's chi-square test. However, in a few analyses the P-value was determined using Fisher's exact test for relevant comparisons. The purpose of this statistical analysis was to assess the significant differences in observed GWU in relation to mentioned variables. The binary outcome variables are modeled using logistic regression and odds ratios were calculated for each predictor variable in the model using SPSS.

RESULTS

In this prospective study, 368 patients, comprising 126 (34.2%) men and 242 (65.8%) women, with a mean age of 58.0 ± 12.5 years (range 15 to 98), were allocated to one of three primary groups. Of all patients enrolled in the study, 114 individuals (31%) were part of the control group (i). Forty-eight individuals (13.1%) were classified into the second group (ii). A total of 206 patients (55.9%) were previously using medications to inhibit gastric acid secretion, with 172 (46.7%) using PPIs (iiia) and 34 (9.2%) using histamine receptor blockers (iiib), but they had discontinued these medications according to our department's current protocol, within one week prior to the scan day. Figure 1 demonstrates that there is no significant difference in the frequency of GWU (score 1, 2 or 3) among all four groups of patients (P value = 0.499).

Table 1 presents the baseline characteristics of all enrolled patients. There were no statistically significant differences observed among the patients in the four groups regarding age, gender

distribution, BMI, diabetes mellitus, hypertension, and hyperlipidaemia (P >0.05)

In the group of patients who were taking PPIs and had discontinued them before the day of the scan, the GWU score of 2 or 3 (n=8, 4.6%) is observed more frequently than in the other groups. Conversely, in the group of patients who were taking PPIs and had not discontinued them prior to the day of the scan, the score of 1 is observed more frequently (n=9, 18.7%) compared to the other groups. However, the statistical analysis revealed no significant variation in the percentage of patients exhibiting any gastric wall uptake (scores of 1, 2, or 3) across all four patient groups (Figure 3) (P value = 0.767). A gastric wall uptake score of 2 or 3 was detected in 13 patients (3.5%), while a score of 1 was observed in 53 patients (14.4%). Among all patients examined, a score of 0 was found in 302 patients (82.1%).

Table 1. Summary of baseline characteristics of all included patients

Characteristics	Control (i) (n=114)	Continued (ii) (n=48)	Discontinued (iii) (n=206)		P value
			PPIs (n=172)	H_2 blockers (n=34)	
Age (years) ± SD (range)	57.40 ± 14.55	58.83 ± 14.08	58.20 ± 10.88	57.88 ± 10.60	0.915
Gender (Female: n(%), Male: n(%))	68(59.6) 46(40.4)	29(60.4) 19(39.6)	121(70.3) 51(29.7)	24(70.6) 10(29.4)	0.216
BMI ± SD (Kg/m2)	27.69 ± 4.50	28.43 ± 4.71	28.77 ± 4.28	27.19 ± 5.04	0.110
Diabetes mellitus n(%)	39(34.2)	18(37.5)	56(32.6)	5(14.7)	0.132
Hypertension n(%)	58(50.9)	29(60.4)	101(58.7)	17(50.0)	0.459
Hyperlipidemia n(%)	46(40.4)	25(52.1)	90(52.3)	18(52.9)	0.208

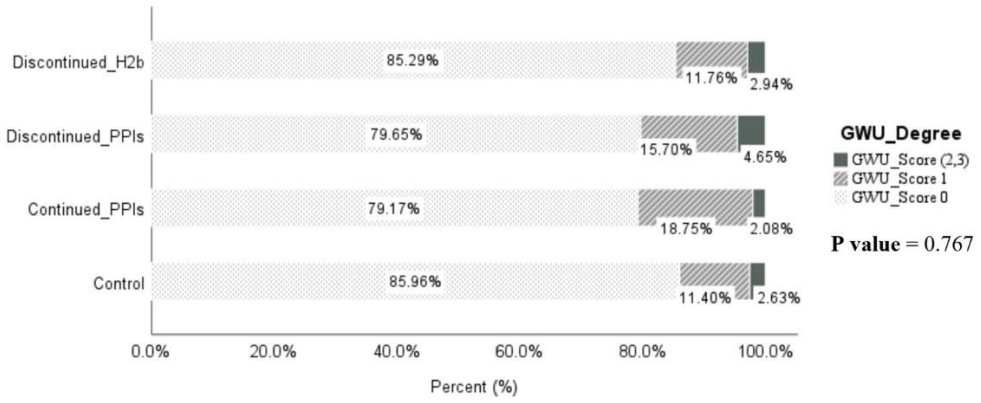

Figure 3. Stacked chart showing no significant difference in gastric wall uptake (GWU) among the patients belonging to different groups in the study population

In the univariable analysis, none of the variables such as gender (P=0.908), diabetes (P=0.593), hypertension (P=0.834), and hyperlipidaemia (P=0.568) showed significant effects on the presence of gastric wall uptake (GWU) in MPI scans.

The patients in subgroup (iiia) were randomly divided for additional sub-analysis, focusing on the duration of PPIs intake. It was observed that there was a higher incidence of gastric wall uptake (GWU) in patients who had been taking PPIs for more than one year (n=29; 22.7%) compared to those who had been taking PPIs for less than one year (n=21; 16.7%). However, this difference did not reach statistical significance (P= 0.232) according to the findings presented in Table 2.

There was no statistically significant difference in the analysis between the subgroups of group (iiia), patients who discontinued their PPIs medication for three days or less compared to those who discontinued it for more than three days (P=0.591) and OR=1.248 and similar findings for one day discontinue and more than one day discontinue were observed (P=0.285) and (OR=1.493) (Table 2, Figures 4 and 5).

The odds ratios for four study groups in this analysis were obtained as follows: group (i) base=1, group (ii) OR=1.506, group (iiia) OR=1.612, group (iiib) OR=1.565, and while all three groups show a positive association, none of them had significant differences on the presence of GWU (Table 2).

The statistical analysis did not demonstrate a significant difference (P=0.672) within subgroup (iiia) between patients who were taking omeprazole or pantoprazole and had discontinued their medication at the time of the scan (Figure 6).

Table 2. Performing univariable analysis to identify correlations between gastric wall uptake (GWU) and patients' variables

Variables	GWU(+) n(%)	Odds Ratio		P value
		Base	95% Con. interval	
Gender (Female / Male)	43(17.8) / 23(18.3)	1 / 1.033	0.591 - 1.808	0.908
Non-Diabetic / Diabetic	43(17.2) / 23(19.5)	1 / 1.165	0.665 - 2.044	0.593
No Hypertension / Hypertension	30(18.4) / 36(17.6)	1 / 0.944	0.553 - 1.613	0.834
Healthy cholesterol level / Hyperlipidaemia	36(19.0) / 30(16.8)	1 / 0.856	0.501 - 1.460	0.568
PPIs intake < 1 Year / PPIs intake ≥ 1 Year	21(16.7) / 29(22.7)	1 /1.465	0.784 - 2.737	0.232
PPIs Discontinue ≤ 3 Days / PPIs Discontinue > 3 Days	30(18.6) / 10(22.2)	1 / 1.248	0.557 - 2.796	0.591
PPIs Discontinue ≤ 1 Days / PPIs Discontinue > 1 Days	14(24.1) / 26(17.6)	1 / 1.493	0.716 - 3.115	0.285
Study Groups				
Control	16(14.0)	1		
PPIs Discontinued	35(20.3)	1.612	0.672 - 3.864	0.285
H2b Discontinued	5(14.7)	1.565	0.820 - 2.985	0.174
PPIs Intake	10(20.8)	1.056	0.356 - 3.129	0.922

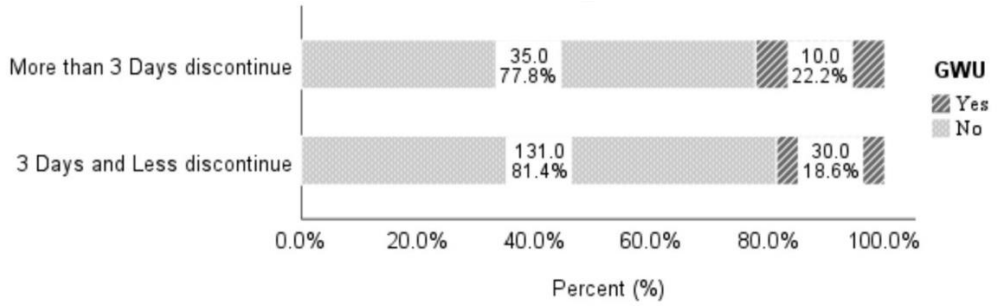

Figure 4. Stacked chart showing no significant difference in gastric wall uptake (GWU) among the patients with 3 days discontinuing of PPIs or more than 3 days in sub-group (iiia)

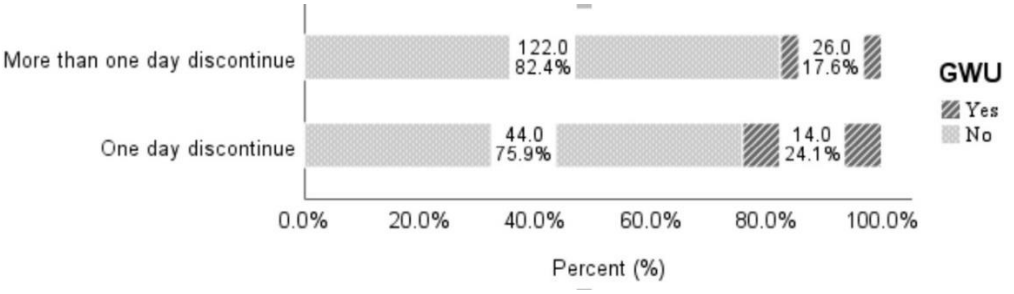

Figure 5. Stacked chart showing no significant difference in gastric wall uptake (GWU) among the patients with one days discontinuing of PPIs or more than one day in sub-group (iiia)

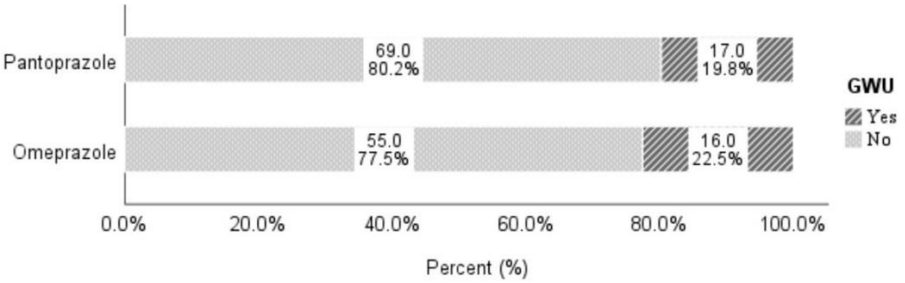

Figure 6. Stacked chart showing no significant difference in gastric wall uptake (GWU) among the patients with Omeprazole and Pantoprazole in sub-group (iiia)

DISCUSSION

The available research on the uptake of [^{99m}Tc]Tc-MIBI in myocardial perfusion within the gastric wall is relatively sparse, and the published studies often involve a limited number of subjects. A comprehensive investigation conducted by Gholamrezanezhad et al. in 2006, involving 1056 patients, found that only 1.9% of the patients displayed high activity in the gastric wall [18]. The low prevalence of activity accumulation in the gastric wall stands in contrast to the high prevalence reported in the studies of Goal et al. [19], Mouden et al. [14], and Singh et al. [20]. In two relatively small prospective observational studies, the comparison of activity accumulation in the gastric wall of patients showed no significant association with discontinuation of H2 antagonists, while an increase in activity accumulation in the gastric wall was strongly correlated with the use of PPIs (Figure 7) [14, 19]. In Goel and colleagues' observational study, 21 individuals (81%) of 26 patients who were under PPIs treatment showed activity accumulation in the gastric wall. In contrast, only 9 out of 95 patients (9%) who did not receive PPIs demonstrated activity accumulation in the gastric wall, indicating a significant difference in terms of observed activity in the gastric wall in these two groups ($p < 0.01$)[19]. While in our study, only 10 out of 48 patients who had used PPIs (20.8%) exhibited activity accumulation in the gastric wall, which is significantly lower compared to the study by Goel et al. [19]. Additionally, among the 114 control group patients who did not use PPIs, 16 individuals (14%) showed activity accumulation in the gastric wall, which is higher than Goel's study (9%). However, statistically, no significant difference was found between individuals who were taking PPIs on the day of the scan and the control group patients in our study ($P > 0.05$).

In another similar study, which involved 127 patients undergoing scanning with the radiopharmaceutical [^{99m}Tc]Tc-tetrofosmin, the number of patients who exhibited activity accumulation in their gastric wall was higher in those who were taking PPIs (22%) compared to those who were not (7%), and a significant difference ($p=0.017$) was observed between the two groups in terms of observed activity in the gastric wall [14].

In another study by Singh et al., a prospective investigation was carried out on 156 patients (both with and without treatment with PPIs and H2 antagonists) [20]. This study involved 47 patients using PPIs, 19 patients using H2 antagonist medications, and an intervention group of 42 patients who were advised to stop their PPI medication three days before the MPI scan.

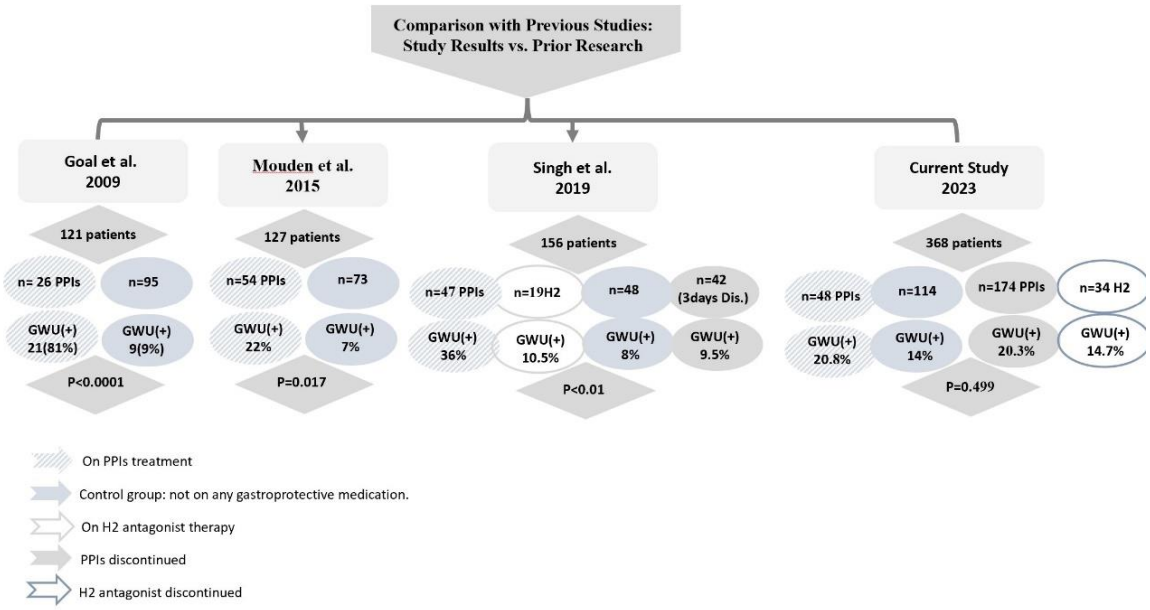

Figure 7. Infographic: comparing the results of the current study with previous research findings

The findings of this study aligned with previous research, indicating that patients who had taken PPI medications showed a higher prevalence of activity accumulation in the gastric wall compared to those on H2 antagonist medications. Activity accumulation in the gastric wall was observed in 36% of patients on PPIs, while only 8% in the control group exhibited activity accumulation, and the difference between these two groups was statistically significant [20]. While in our study, the percentage of patients with activity accumulation in their gastric wall was 20.8% compared to 36% in Singh's study, indicating a significantly lower prevalence. In our investigation, we focused on assessing the accumulation of radioactivity in the gastric wall during the resting phase, as it tends to be consistently more pronounced in contrast to the exercise phase [22]. On the other hand, the percentage of patients in the control group in our study who exhibited activity accumulation (14%) was higher compared to 8% in Singh's study. Singh et al. mentioned that there was no statistically significant difference between the group of patients who had discontinued PPI medication three days prior to the scan (5.9%) and the control group that had not been under PPI treatment from the beginning (8%) (P=0.84) [20]. In our study, it was evident that among the 156 patients who had discontinued their PPI medication three days or less before the MPI scan, 29 individuals (18.6%) exhibited radiopharmaceutical uptake in the gastric wall. On the other hand, out of the 46 patients who had discontinued their PPI medication for more than three days, only 10 individuals (21.7%) showed gastric wall radiopharmaceutical uptake, indicating a statistically non-significant difference (P=0.634). However, the statistical analysis result for the two patient groups, those who discontinued their medication for one day or less and those who discontinued for more than one day, also did not show a significant difference. Out of the 54 patients who had discontinued their PPI medication for one day or less, 13 individuals (24.1%) exhibited activity accumulation in the gastric wall, while 26 out of 147 patients who had discontinued the medication for more than one day (17.7%) showed activity accumulation (P=0.310).

The study examined the activity accumulation in the stomach walls of patients who discontinued their PPI medication, categorizing them into two groups based on different durations of medication use (more than one year and less than one year). The statistical analysis showed no significant difference in activity accumulation between the two groups (P>0.05), suggesting that prolonged use of PPIs did not significantly contribute to activity accumulation in the stomach wall. This contradicts the claims of Rose et al., who suggest that long-term PPI intake, leading to hypergastrinemia, acts as a cell growth factor, contributing to increased perfusion and MIBI uptake in the gastric wall [23].

In contrast to prior studies using planar imaging to identify activity accumulation in the stomach walls, our research employed SPECT images co-registered with CT scans [15]. Relying solely on planar images introduced potential inaccuracies in pinpointing the exact location of activity. Initial observations on planar images suggested gastric wall activity, but subsequent analysis with SPECT/CT images clarified that the observed activity was related to uptake in intestinal and, in some cases, hepatic lobes (Figure 8). Thus, for more precise localization and differentiation of gastric wall activity from other sites, we recommend the utilization of SPECT/CT imaging in future studies.

The difference in reported odds ratios between our study (OR=1.056, P=0.922) and that of other researchers (OR=6.233, P=0.002 [17] and OR=6.31, P<0.001[15]) regarding the association between PPIs use and gastric wall uptake (GWU) suggests a considerable disparity in findings. Methodological variations, including differences in study populations, definitions of outcomes, or sample sizes, may contribute to this discrepancy. Understanding these differences is vital for a thorough interpretation, highlighting the importance of standardized methodologies and additional investigation to enhance our comprehension of the association between PPIs usage and GWU.

Our study discovered non-significant differences in gastric wall activity among patients actively using PPI medication, those who had discontinued it on the scan day, and the control group. Considering the challenges associated with discontinuing PPIs for many patients and the operational difficulties of pre-screening individuals, particularly in emergency or hospitalized situations, healthcare facilities face significant hurdles. This underscores the necessity for further research to comprehensively understand the impact of PPIs consuming on the gastric wall uptake.

Two mechanisms for the accumulation of radiotracer in the gastric wall in patients undergoing PPIs therapy have been mentioned in the literature. On one hand, Goel et al. have proposed that PPIs inhibit radiotracer secretion by

suppressing the sodium-potassium pump, leading to the retention of radiotracer in numerous mitochondria of parietal cells in the gastric wall [19]. Considering the chemical structure of the [^{99m}Tc]Tc-MIBI complex, which is a large lipophilic cation, and passes through cells membranes passively via phospholipids. The distribution and delivery to tissues depend on regional blood flow, mitochondrial membrane potential, and mitochondrial content [24]. Therefore, it is unlikely that PPIs could affect the transit and accumulation of this complex within the parietal cells of the gastric wall. On the other hand, Rose and collaborators have suggested that long-term use of PPIs induces hypergastrinemia, acting as a cell growth factor, thereby increasing perfusion and activity in the gastric wall [16].

According to the findings of our study, there is no necessity to discontinue the use of PPIs for myocardial perfusion scans. However, for centers that insist on discontinuation, it might be advisable to discontinue PPI medications for just one day before the scan, as opposed to long-term cessation of PPIs, especially for patients with active gastric ulcers or those who have recently undergone a surgery.

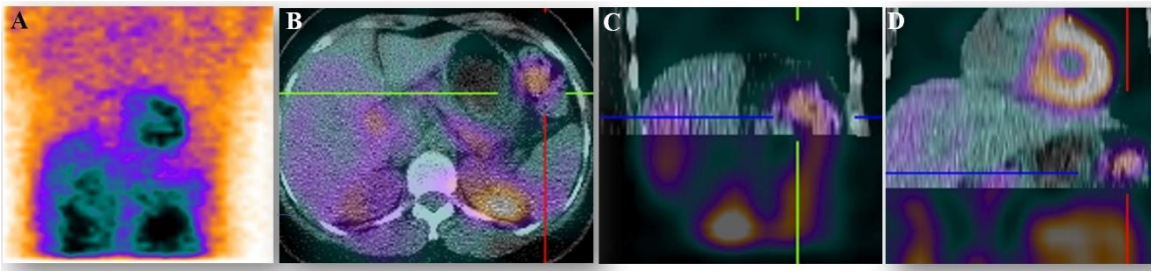

Figure 8. Initial planar imaging indicates gastric wall activity (A), Subsequently clarified by SPECT/CT (B, C, D): Noted uptake in the intestines

Study limitations

The timing of scans following radiopharmaceutical injection is not consistently uniform in our centre due to existing constraints, which might potentially introduce some interpretation errors. To minimize these errors, the assessment of gastric wall radiopharmaceutical uptake was conducted using SPECT/CT images, providing a much more precise determination of the location of activity as compared to planar images.

CONCLUSION

The study found no significant link between the use of PPIs and activity accumulation in the gastric wall during myocardial perfusion imaging scans. It suggested that a 24-hour discontinuation of PPIs before the scan might be a sufficient cessation time interval. The precise anatomical site of interference in myocardial perfusion scans was identified through SPECT/CT images. While PPIs usage may pose challenges in interpreting inferior wall scan results, further multicentre studies with larger patient populations and the use of SPECT/CT images are needed to determine the impact of PPIs on activity uptake in the gastric wall during myocardial perfusion imaging.

Acknowledgements

The authors extend they're thanks to Mrs. Leila Sari of the Nuclear Medicine Centre at Rajaee Cardiovascular Medical and Research Centre for her wholehearted collaboration in gathering patient information cases for this study.

REFERENCES

1. Zaret BL, Beller GA. Clinical nuclear cardiology: state of the art and future directions. 4th ed. Elsevier. 2010. p. 4-5.
2. Janis P. O'Malley HAZ. Nuclear medicine and molecular imaging: the requisites. 5th ed. Elsevier. 2020. p. 449-50.
3. Piwnica-Worms DP, Kronauge JF, LeFurgey A, Backus M, Hockett D, Ingram P, Lieberman M, Holman BL, Jones AG, Davison A. Mitochondrial localization and characterization of 99Tc-SESTAMIBI in heart cells by electron probe X-ray microanalysis and 99Tc-NMR spectroscopy. Magn Reson Imaging. 1994;12(4):641-52.
4. McNulty EJ, Hung YY, Almers LM, Go AS, Yeh RW. Population trends from 2000-2011 in nuclear myocardial perfusion imaging use. JAMA. 2014 Mar 26;311(12):1248-9.
5. Jain D, Lessig H, Patel R, Sandler L, Weiland F, Edell SL, Elizabeth Oates M, O'Malley-Tysko E, Khutoryansky N, Jacobson AF. Influence of 99mTc-tetrofosmin SPECT myocardial perfusion imaging on the prediction of future adverse cardiac events. J Nucl Cardiol. 2009 Jul-Aug;16(4):540-8.
6. Burrell S, MacDonald A. Artifacts and pitfalls in myocardial perfusion imaging. J Nucl Med Technol. 2006 Dec;34(4):193-211; quiz 212-4.

7. Peace RA, Lloyd JJ. The effect of imaging time, radiopharmaceutical, full fat milk and water on interfering extra-cardiac activity in myocardial perfusion single photon emission computed tomography. Nucl Med Commun. 2005 Jan;26(1):17-24.
8. Boz A, Yildiz A, Güngör F, Karayalçin B, Erkiliç M. The volume effect of the stomach on intestinal activity on same-day exercise--rest Tc-99m tetrofosmin myocardial imaging. Clin Nucl Med. 2001 Jul;26(7):622-5.
9. Germano G, Chua T, Kiat H, Areeda JS, Berman DS. A quantitative phantom analysis of artifacts due to hepatic activity in technetium-99m myocardial perfusion SPECT studies. J Nucl Med. 1994 Feb;35(2):356-9.
10. Hofman M, McKay J, Nandurkar D. Efficacy of milk versus water to reduce interfering infra-cardiac activity in 99mTc-sestamibi myocardial perfusion scintigraphy. Nucl Med Commun. 2006 Nov;27(11):837-42.
11. Hambÿe AS, Delsarte P, Vervaet AM. Influence of the different biokinetics of sestamibi and tetrofosmin on the interpretation of myocardial perfusion imaging in daily practice. Nucl Med Commun. 2007 May;28(5):383-90.
12. Haghighatafshar M, Sarfaraz A, Banani A, Farhoudi F, Etemadi Z. The effect of pomegranate juice, lemon juice and secanjabin in reducing infra-cardiac activity of 99mTc-MIBI during myocardial perfusion imaging in comparison with fatty food. Iran J Nucl Med. 2019;27(2):113-117.
13. Hendel RC, Corbett JR, Cullom SJ, DePuey EG, Garcia EV, Bateman TM. The value and practice of attenuation correction for myocardial perfusion SPECT imaging: a joint position statement from the American Society of Nuclear Cardiology and the Society of Nuclear Medicine. J Nucl Cardiol. 2002 Jan-Feb;9(1):135-43.
14. Mouden M, Rijkee KS, Schreuder N, Timmer JR, Jager PL. Influence of proton-pump inhibitors on stomach wall uptake of 99mTc-tetrofosmin in cadmium-zinc-telluride SPECT myocardial perfusion imaging. Nucl Med Commun. 2015 Feb;36(2):143-7.
15. Norouzi G, AsadZade A, Salimi Y, Khoshbakht S, Pirayesh E. Effect of proton pump inhibitors and H2 antagonists on gastric wall uptake in myocardial perfusion scan with 99mTc-sestamibi. J Nucl Cardiol. 2022 Aug;29(4):1552-61.
16. Rose DS, Robinson B, Kannan S, Lee JC. Interaction between the effects of proton pump inhibitors and aspirin on gastric wall sestamibi uptake on myocardial perfusion imaging. J Nucl Cardiol. 2021 Oct;28(5):1976-85.
17. Sood A, Singh H, Bollampally N, Gorla AK, Parmar M, Dasagrandhi V, Mittal B. Association of gastric wall tracer uptake with proton pump inhibitor use in patients undergoing 99mTc-sestamibi myocardial perfusion scintigraphy. J Nucl Med. 2019 May; 60 (supplement 1) 1423.
18. Gholamrezanezhad A, Moinian D, Eftekhari M, Mirpour S, Hajimohammadi H. The prevalence and significance of increased gastric wall radiotracer uptake in sestamibi myocardial perfusion SPECT. Int J Cardiovasc Imaging. 2006 Jun-Aug;22(3-4):435-41.
19. Goel S, Bommireddipalli S, DePuey EG. Effect of proton pump inhibitors and H2 antagonists on the stomach wall in 99mTc-sestamibi cardiac imaging. J Nucl Med Technol. 2009 Dec;37(4):240-3.
20. Singh H, Mittal BR, Sood A, Bollampally N, Gorla AKR, Dasagrandhi V, Parmar M. Association of use of proton pump inhibitors and H_2 antagonists with stomach wall uptake in ^{99m}Tc-methoxy-isobutyl-isonitrile (MIBI) myocardial perfusion imaging. J Nucl Cardiol. 2020 Oct;27(5):1611-19.
21. Henzlova MJ, Duvall WL, Einstein AJ, Travin MI, Verberne HJ. ASNC imaging guidelines for SPECT nuclear cardiology procedures: Stress, protocols, and tracers. J Nucl Cardiol. 2016 Jun;23(3):606-39.
22. Côté C, Dumont M. The clinical meaning of gastric-wall hyperactivity observed on sestamibi cardiac single-photon emission computed tomography. Can Assoc Radiol J. 2004 Jun;55(3):178-83.
23. Rose DS, Robinson B, Kannan S, Lee JC. Interaction between the effects of proton pump inhibitors and aspirin on gastric wall sestamibi uptake on myocardial perfusion imaging. J Nucl Cardiol. 2021 Oct;28(5):1976-85.
24. Rizk TH, Nagalli S. Technetium 99m Sestamibi. 2023 Jul 3. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan–. PMID: 31985941.