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Increased Stomach Activity on Myocardial Perfusion Imaging

Grace Brayshaw[1], Sharon Mosley[2] & Geoff Currie[1,3]

[1]Faculty of Science, Charles Sturt University, Wagga Wagga, Australia
[2]Department of Nuclear Medicine, The Canberra Hospital, Canberra, Australia
[3]Faculty of Medicine and Health Sciences, Macquarie University, Sydney, Australia

Corresponding author:
Geoff Currie
School of Dentistry and Health Sciences
Locked Bag 588
Charles Sturt University
Wagga Wagga NSW 2678
61 2 69332822
gcurrie@csu.edu.au

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ABSTRACT

Introduction: Anecdotal observation was made of increased stomach accumulation of 99mTc Tetrofosmin in myocardial perfusion patients where the uptake phase corresponded to the preparation of hamburgers for gastric empty patients. The potential for olfactory stimulation of altered gastric biodistribution required further investigation.

Methodology: An experimental group and a control group of patients were recruited (n=20 each). The experimental group could smell food preparation in the adjacent room during the uptake phase. Stomach, heart and background regions were drawn in multiple projections and the resulting data evaluated.

Results: There was no statistically significant difference between the experimental and control groups for stomach counts per pixel, background corrected counts per pixel or the heart to stomach ratio. Further analysis of the data revealed a statistically significant increase in stomach counts (P=0.022) and background corrected stomach counts (P=0.018) for females over males.

Conclusion: While there is no causal relationship between increased stomach activity of 99mTc tetrofosmin and olfactory stimulation from cooking food during the uptake phase of the radiopharmaceutical, increased stomach accumulation can be attributed to female gender.

Introduction

Anecdotal observation of a number of instances of increased stomach accumulation of 99mTc Tetrofosmin in myocardial perfusion patients prompted further investigation (figure 1). Several instances of the same observation were noted to occur on the same period of (adjacent physical spaces) myocardial perfusion patients uptake phase and gastric empty patients had hamburger meals prepared. The potential for olfactory stimulation of altered gastric biodistribution required further investigation.

Despite the benefits of myocardial perfusion imaging, image quality continues to suffer a number of artefacts (*1,2*). Radiopharmaceutical artefatcs are more difficult to manage than technical errors. 99mTc-Tetrofosmin not only localises within the heart, but it also localizes in other pathologies (eg. soft tissue tumours) and organs (eg. liver, gallbladder, stomach and bowel). This can become problematic, especially where aberrant activity overlies the myocardium.

The impact of the scent of food on 99mTc-Tetrofosmin biodistribution has not been previously reported in the literature. Indeed, olfactory stimulation during the uptake phase of the radiopharmaceutical in a fasted patient may have a significant impact on biodistribution. During the cephalic phase of digestion (occurring, when the scent, sight, taste or thought of food is present), it has been demonstrated that there is a significant increase of gastric acid secretions induced by the vagus nerve. These secretions include; pepsinogen, gastrin, hydrochloric acid (HCL) and other digestive enzymes (*3*). The final step of hydrochloric acid production involves the H^+/K^+/ATPase proton pump (*4*). This pump utilises the energy of ATP to counter transport H^+ out of the cell and K^+ ions across the cell membrane (*4*). The mechanism of uptake of 99mTc – Tetrofosmin in stomach tissue is unknown. It has been suggested that 99mTc – Sestamibi localises in the mitochondria of parietal cells and is excreted via the H^+/K^+ ATPase pump into the gastric lumen (*5,6*) and, therefore, has been hypothesised that 99mTc - Tetrofosmin may localise in a similar manner (*6*).

99mTc - Tetrofosmin activity from the stomach can also be attributed to pathologies such as dyspepsia, gastritis and enterogastric bile reflux (*7,8*). Gholamrezanezhad et al. (*7*) conducted a study involving 1056 myocardial perfusion patients, although they found a low incidence of gastric wall uptake, the authors concluded that most patients with these uptake patterns were associated with dyspeptic symptoms. These findings are consistent with a previous study by Côte & Dumont (*8*), who identified gastric wall hyperactivity in 13 of 819 patients due to known dyspepsia. Several case studies (*9-11*) have also demonstrated significant activity in the stomach wall or cavity during myocardial perfusion imaging due to gastrointestinal pathologies.

It has been proposed that medications such as histamine2 (H2) antagonists and proton pump inhibitors (PPI) may also increase activity in the stomach during myocardial perfusion imaging (*12*). Mouden et al. (*6*) investigated stomach wall uptake in myocardial perfusion patients who have taken PPIs or H2 antagonists over a prolonged period of time and demonstrated 17 of 127 patients to have clinically relevant gastric uptake of 99mTc – tetrofosmin.

Methods

The purpose of this study was to retrospectively quantitate stomach activity in patients having myocardial perfusion stress testing who were exposed to the smell of cooking hamburgers during the uptake phase compared to a control group. 20 consecutive patients were recruited for each of the experimental and control groups. Both hospital and university institutional ethics approvals were obtained.

Patients are required to have met several preparation requirements before presenting to the department including; cessation of medications that interfere with the study (where possible), abstinence of caffeine products for 24 hours prior to the study, and fasting from midnight or at least 4 hours prior to study (with the exception of diabetics). These also represented inclusion/exclusion criteria for this study.

All patients underwent a 1 day rest (350 MBq) / stress (1000 MBq) protocol with 30-50 min delay between radiopharmaceutical (99mTc - tetrofosmin) administration and commencement of imaging. The patients were positioned supine with the camera in cardiac configuration (L) mode and both SPECT and low dose CT images acquired. The SPECT images are obtained on a 64 x 64 matrix with 22 seconds per step. The low dose CT image was used for the purpose of attenuation correction, and is acquired using a kV of 140, mA of 1, and a pitch of 1.9.

For the experimental group, during the delay between radiopharmaceutical administration and imaging, the patients were seated in the waiting room adjacent to the area in which meals were prepared for the gastric emptying procedures. The meal prepared was a hamburger comprised of 100g beef, a bun with lettuce, tomato and egg, and any dressings the patient may request (eg. mayonnaise, salt, pepper or tomato sauce). Only the egg was cooked within the department, however, the bun was toasted and meat heated. Anecdotal observation suggests that the reheating of the meat was the primarily olfactory stimulation in the patient waiting area.

The raw data acquired during rest imaging was analysed using the GE healthcare's Xeleris software program. Planar projections at 0°, 22.5° and 45º angles obtained from the maximum intensity projection (MIP), were used with regions of interest (ROIs) drawn around the stomach, heart and soft tissue background to determine count rates. The ROIs were drawn at 3 angles in order to correct for motion and each ROI was also redrawn 3 times. Raw mean and background corrected mean counts per pixel were determined and the ratio of heart to stomach calculated.

For nominal data, statistical significance was calculated using Chi-Square analysis while the Student's *t* test was used for continuous data. Grouped data was evaluated using the *F* test analysis of variances. A *P* value less than 0.05 was considered significant. The differences between independent means were calculated with a 95% confidence interval (CI). Inter-value correlation was evaluated with Chi-Square analysis and inter-value reliability measured using Cohen's Kappa coefficient. A matched pairs *t* test evaluated statistically significant correlations between paired data.

Results

Overall, 40 patients were recruited with 22 male (55%) and 18 female (45%). The mean age of the population was 61 years with a 95% CI of 56.7-65.7 years and a range 27-87 years. Across the 2 cohorts, the mean background counts per pixel was 28.6 with a 95% CI 25.5 – 31.7 and a range of 16.0-57.9. Similarly, the overall mean heart counts per pixel was 105.3 with a 95% CI 88.2 – 122.3 and a range of 44.5-287.0. For stomach counts per pixel, the mean was 105.3 with a 95% CI 80.3 – 105.3 and a range of 10.5-429.9. The overlap in 95% CIs indicates no statistically significant difference between heart and stomach counts per pixel in the group as a whole. This remained true for the background corrected counts per pixel. The mean background corrected heart counts per pixel was 76.6 with a 95% CI 62.0 – 91.2 and a range of 23.7-240.2. The mean background corrected stomach counts per pixel was 76.6 with a 95% CI 53.1-100.2 and a range of -28.0 to 383.0. The mean background corrected ratio of heart : stomach was -0.15 with a 95% CI -2.82 to 2.51 and a range of -46.9 to 11.2.

An evaluation of the experimental group compared to the control group revealed no statistically significant differences (table 1). There was a much larger representation of females in the control group than the experimental group which may confound the data, despite no statistically significant difference (P=0.06). Importantly, there was no statistically significant difference between the experimental and control groups for stomach counts per pixel, background corrected counts per pixel or the heart to stomach ratio. Indeed, the mean counts per pixel was lower in the experimental group compared to the control group and this is likely to reflect the gender distribution.

A closer examination of the parameters with respect to gender (table 2) revealed no statistically significant difference in age, background or heart. It did, however, reveal a statistically significant increase in stomach counts (P=0.022) (figure 2) and background corrected stomach counts (P=0.018) (figure 3) for females. The disproportionate representation of females in the control group is likely to explain the skewed data outlined in table 1. Elimination of a potential outlier (figures 2 and 3) did not alter this finding with statistically significant increases for both stomach (P=0.038) and background corrected stomach (P=0.029).

No statistically significant relationship was demonstrated between age and either background, heart, stomach, background corrected heart, background corrected stomach or the heart to stomach ratio (all P>0.17 and $R^2 < 0.05$). No statistically significant differences were noted between ROIs (intra operator variability(P>0.157 and correlation > 0.99). There were also no differences noted between distribution of counts based on angular projection at which they were drawn (P>0.748), however, statistically higher counts were noted (as expected) for both 22.5 and 45 degrees over 0 degrees and 45 degrees over 22.5 degrees (P < 0.04).

Discussion

This study provides a number of important findings and observations. Firstly, the anecdotal observation that olfactory stimulation during the uptake phase of 99mTc tetrofosmin might increase stomach accumulation of the radiopharmaceutical has been shown to be untrue. Secondly, in consideration of this finding, noting was made that the first few cases that aroused the suspicion that the smell of hamburger increased stomach activity were all in females. This was supported by a statistically significant relationships between female gender and increased stomach counts (including after background correction). The mechanism of this phenomena is unclear, however, it is likely to relate to hormone driven changes in gastrointestinal function. Previous studies have shown slower gastric transit in women over men and this finding is independent of pregnancy status or phase of the menstrual cycle (*13*). This implies that it is not the concentration of sex hormone that is important but rather simply the presence of them. The sex hormones are thought to impact on a number of hormones, receptors and enzymes that impact on digestion and, as discussed above, these enzymes can increase stomach uptake of 99mTc tetrofosmin. It is possible that the observation simply relates to increased prevalence of the previously discussed pathologies that could increased stomach uptake of 99mTc tetrofosmin, however, data on co-morbidity was not available. Interestingly, there was a weak positive correlation between age and stomach counts in females that extended beyond the menopause window ($R^2 = 0.16$ or 16% of the increase in stomach counts can be attributed to age). This observation was not seen in males ($R^2 = 0.003$).

The third key finding from this study relates to the justification for research amongst medical radiation technologists. Policy and decision making can be undertaken on the basis of anecdotal observation and, in some cases, relationships appear consistent. Nonetheless, what we observe should also be rigorously evaluated with appropriately structured research. Research is within both the scope of practice and capability of the medical radiation technologist and, indeed, there is a responsibility to engage and undertake research. This study provides an insight into why this is an essential role of the medical radiation technologist. Problem solving is most effective when all details are known rather than based on observation or assumptions. Simple through to complex problems or variations are occur frequently with daily practice and these provide suitable fodder for technologist driven research. The outcomes better inform and improve patient outcomes. The other key research insight is to account for confounders. Too often small research projects overlook potential confounders. In this case, gender. A simple project would have identified there was no substance to the anecdotal observation but would fail to link gender as a confounder. While all confounders are difficult to accommodate and a large randomised controlled trial are beyond the scope of many clinical practitioners, this study shows how a simple control group can provide a deeper insight.

Study Limitations

The major limitation of this study is a small population. The imperfect matching of experimental and control groups in this case has provided a deeper insight but represents a limitation. The retrospective nature of the study was prohibitive of gleaning important information on medications and co-morbidity to better explain the gender based differences observed.

Recommendations

Further insight and understanding of the effects of sex hormones on biodistribution of 99mTc tetrofosmin, and other myocardial perfusion agents, is recommended in a more tightly controlled study design.

Conclusion

There is no causal relationship between increased stomach activity of 99mTc tetrofosmin and olfactory stimulation from cooking food during the uptake phase of the radiopharmaceutical. Increased stomach accumulation of 99mTc tetrofosmin may be observed in females compared to males.

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Figure 1: Typical myocardial perfusion rest study (left) with prominant cardiac activity and minimal stomach activity compared to marked stomach accumulation of the radiopharmaceutical (right) for a patient uptake phase during hamburger preparation.

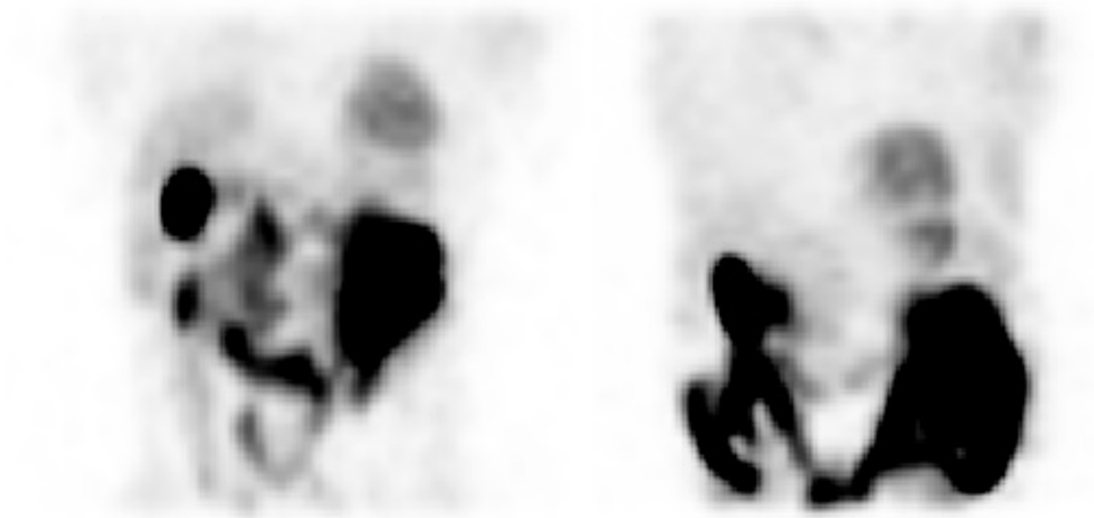

Figure 2: Oneway analysis of the mean stomach counts per pixel against gender.

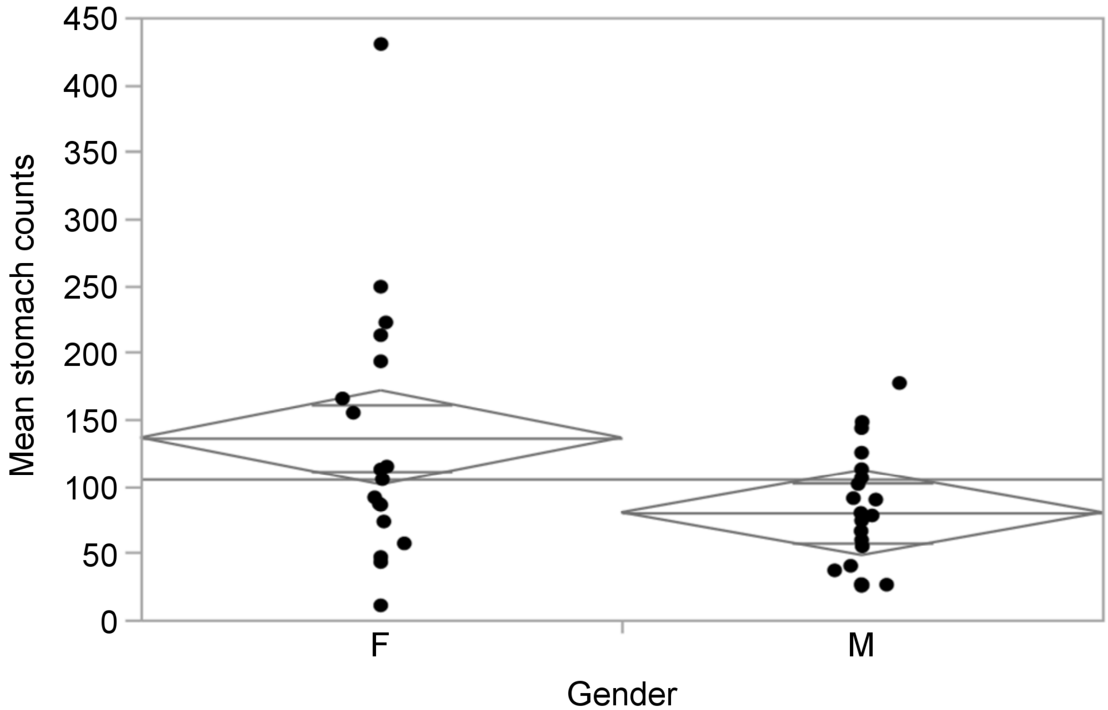

Figure 3: Oneway analysis of the mean background corrected stomach counts per pixel against gender.

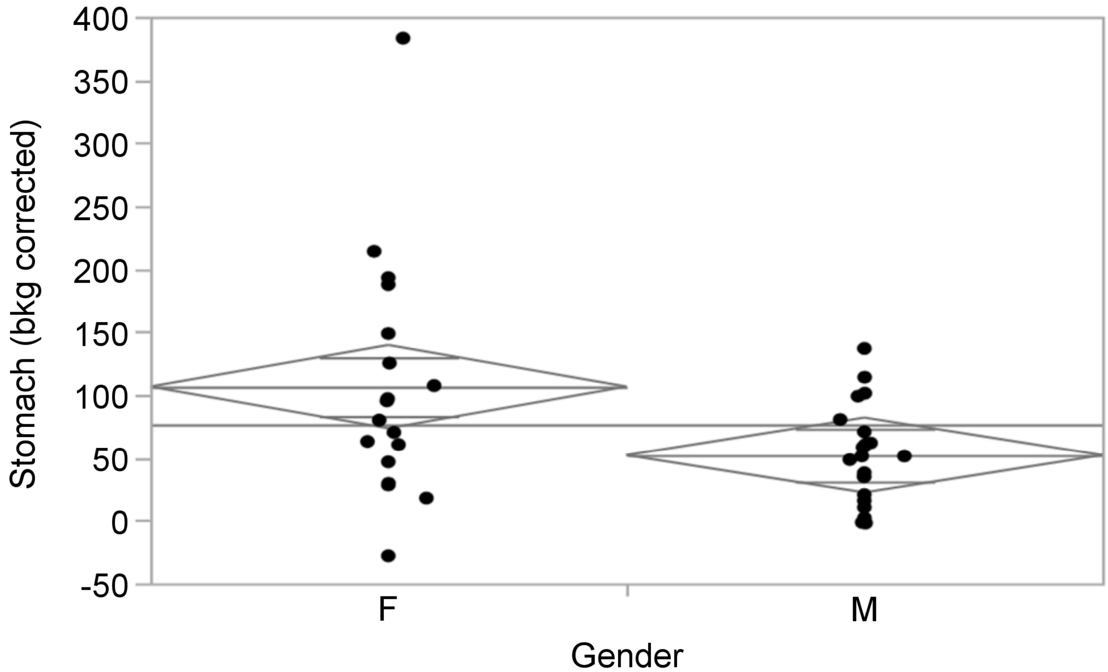

Table 1: Key parameters comparing the control group and the experimental group.

	Control	Experiment	
Number	20	20	
Gender (female)	66.7% females	33.3% females	p=0.06
Age (mean and 95% CI)	60.2 (53.8-66.6)	62.3 (55.8-68.7)	P=0.65
Background CPP	28.4 (24.0-32.9)	28.8 (24.3-33.3)	P=0.91
Heart CPP	107.5 (83.0-132.0)	103.0 (78.5-127.5)	P=0.79
Stomach CPP	111.0 (75.3-146.8)	99.5 (63.7-135.3)	P=0.65
Heart Bkg corrected	79.1 (58.2-100.0)	74.2 (53.2-95.1)	P=0.74
Stomach bkg corrected	82.6 (48.9-116.3)	70.7 (37.0-104.4)	P=0.62
Heart : Stomach	1.23 (-2.53 to 5.00)	-1.54 (-5.31 to 2.23)	P=0.30

Table 2: Key parameters comparing the females and males.

	Females	**Males**	
Age (mean and 95% CI)	59.9 (53.3-66.7)	62.3 (56.2-68.4)	P=0.61
Background CPP	29.6 (24.9-34.2)	27.9 (23.6-32.1)	P=0.59
Heart CPP	110.2 (84.5-136.0)	101.2 (77.9-124.4)	P=0.60
Stomach CPP	136.2 (100.9-171.4)	80.0 (48.1-111.9)	P=0.0218
Heart Bkg corrected	80.7 (58.7-102.7)	73.3 (53.4-93.2)	P=0.62
Stomach bkg corrected	106.6 (73.6-139.6)	52.1 (22.3-82.0)	P=0.0179
Heart : Stomach	0.86 (-3.13 to 4.87)	-0.99 (-4.61 to 2.63)	P=0.49