# ORIGINAL ARTICLE

# Suppressing physiologic 18-fluorodeoxyglucose uptake in patients undergoing positron emission tomography for cardiac sarcoidosis: The effect of a structured patient preparation protocol

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***Objective.*** **Myocardial positron emission tomography (PET) to detect cardiac sarcoidosis requires adequate patient preparation; however, in many cases physiologic myocardial $^{18}$F-fluorodeoxyglucose ($^{18}$F-FDG) uptake may not be adequately suppressed. We sought to evaluate the efficacy of a structured patient preparation protocol as recommended by the joint SNMMI/ASNC expert consensus document on the role of $^{18}$F-FDG PET/CT in cardiac sarcoid detection and therapy monitoring. The SNMMI/ASNC preparation protocol recommends at least two high-fat (> 35 g), low-carbohydrate (< 3 g) (HFLC) meals the day before testing followed by fasting for at least 4-12 hours.**

***Methods.*** **All unique PET scans performed for cardiac sarcoidosis before (group 1) and after (group 2) application of the new preparation protocol were included in the study. In group 1, patients were given a preparation protocol of HFLC meals with suggested meals examples, while patients in group 2 received detailed diet instructions, together with accepted and non-accepted meal examples along. In group 2, reinforcement of instructions by nursing staff and review of dietary log were performed prior to testing. All PET images were evaluated for suppression of physiologic myocardial $^{18}$F-FDG uptake.**

***Results.*** **Group 1 included 124 unique patients, and group 2 included 232 unique patients. There were no significant differences in baseline patient characteristics between the two groups. Suppression of physiologic myocardial $^{18}$F-FDG uptake was achieved in 91% of patients in group 2, compared to 78% of patients in group 1 ($P < .001$). A ''diffuse'' myocardial uptake pattern, indicating inadequate $^{18}$F-FDG suppression, was seen in 2% of studies in group 2 vs 12% in group 1 ($P < .001$).**

***Conclusion.*** **In this single-center study, application of a structured preparation protocol was highly successful in achieving suppression of physiologic myocardial $^{18}$F-FDG uptake in patients undergoing myocardial PET for cardiac sarcoidosis. (J Nucl Cardiol 2021;28:661–71.)**

**Key Words: Cardiac sarcoidosis • positron emission tomography • 18-fluorodeoxyglucose • dietary preparation**

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| Abbreviations | |
|---|---|
| CS | Cardiac sarcoidosis |
| CT | Computed tomography |
| FDG | Fluorodeoxyglucose |
| HFLC | High-fat low-carbohydrate |
| PET | Positron emission tomography |

## INTRODUCTION

Sarcoidosis is an inflammatory disorder of unknown etiology characterized by non-necrotizing granulomas involving one or more organ systems. Approximately 25% of patients with pathology-proven extracardiac sarcoidosis have evidence of cardiac involvement by advanced cardiac imaging,[1] a rate that is consistent with a previously published U.S.-based autopsy study.[2]

Because glucose metabolism is markedly increased in inflammatory cells (such as in granulomas), myocardial inflammation can be detected by $^{18}$F-fluorodeoxyglucose ($^{18}$F-FDG) positron emission tomography (PET). Cardiac $^{18}$F-FDG PET has become an essential tool in the evaluation of suspected or established cardiac sarcoidosis (CS).[3] Since normal cardiomyocytes also use glucose for energy production, suppression of physiologic myocardial $^{18}$F-FDG uptake is critical for visualization of $^{18}$F-FDG uptake by inflammatory cells. The recently published joint SNMMI/ASNC expert consensus document on the role of $^{18}$F-FDG PET in CS detection and therapy monitoring underscored the importance of patient preparation aimed to achieve suppression of physiologic myocardial $^{18}$F-FDG uptake in patients undergoing PET for CS detection.[3] This may be accomplished using several approaches: a fat-enriched diet lacking carbohydrates for 12-24 hours prior to the scan,[4,5] a 12-18-hour fast,[6] and/or the use of intravenous unfractionated heparin approximately 15 minutes prior to $^{18}$F-FDG injection.[7] The expert consensus document acknowledges the substantial variability in these preparation protocols as well as their success rates in achieving suppression of physiologic myocardial $^{18}$F-FDG uptake in published studies. In a recent review of 31 studies assessing various suppression protocols, success rates ranged between 10 and 100%, with the majority of studies having a small sample size.[8] Based on published literature and expert opinion, the joint expert consensus document advocates a combined approach of at least two high-fat (> 35 g), low-carbohydrate (< 3 g) (HFLC) meals the day before the PET study followed by a fast of at least 4-12 hours. The purpose of this study was to compare the differences in the suppression of physiologic $^{18}$F-FDG myocardial uptake between (1) a diet protocol consisting of only HFLC meals and (2) a structured protocol of combined HFLC meals and prolonged fasting with compliance reinforcement and detailed patient instructions.

## METHODS

### Patient Population and Preparation Protocols

The study included consecutive patients who underwent cardiac PET imaging for detection of CS between March 2010 and September 2017 at a single tertiary academic medical center (Mayo Clinic, Rochester, Minnesota). Prior to August 1, 2016 (Group 1), the preparation protocol consisted of only HFLC meals, and patients were asked to eat up until 2 hours before the $^{18}$F-FDG PET study. Patients were contacted only 24 hours prior to the $^{18}$F-FDG PET study. Only one example of an acceptable meal was provided and no instructions were given regarding exercise activities. Starting on August 1, 2016, a new suppression protocol with stricter and earlier instructions was implemented.[9] Differences between the old and new preparation protocols are outlined in Table 1. The new protocol instructed patients to consume at least two HFLC

**Table 1.** Comparison between old and new preparation protocols

| Old protocol (before August 2016) | New protocol (after August 2016) |
|---|---|
| Patients called 24 hours before scan | Patients called 48 hours before scan |
| An example of an acceptable meal is provided | A strict list of permissible options is provided |
| Food allowed after 5 pm the day before scan | Fasting after 5 pm the day before scan |
| High-fat/low-carbohydrate meal 2 hours prior to scan | No meal 2 hours prior to scan |
| No food log required | Food log mandatory |
| Exercise allowed | Exercise not allowed |
| No 18-hour fast given as option | 18-hour fast given as alternative option |

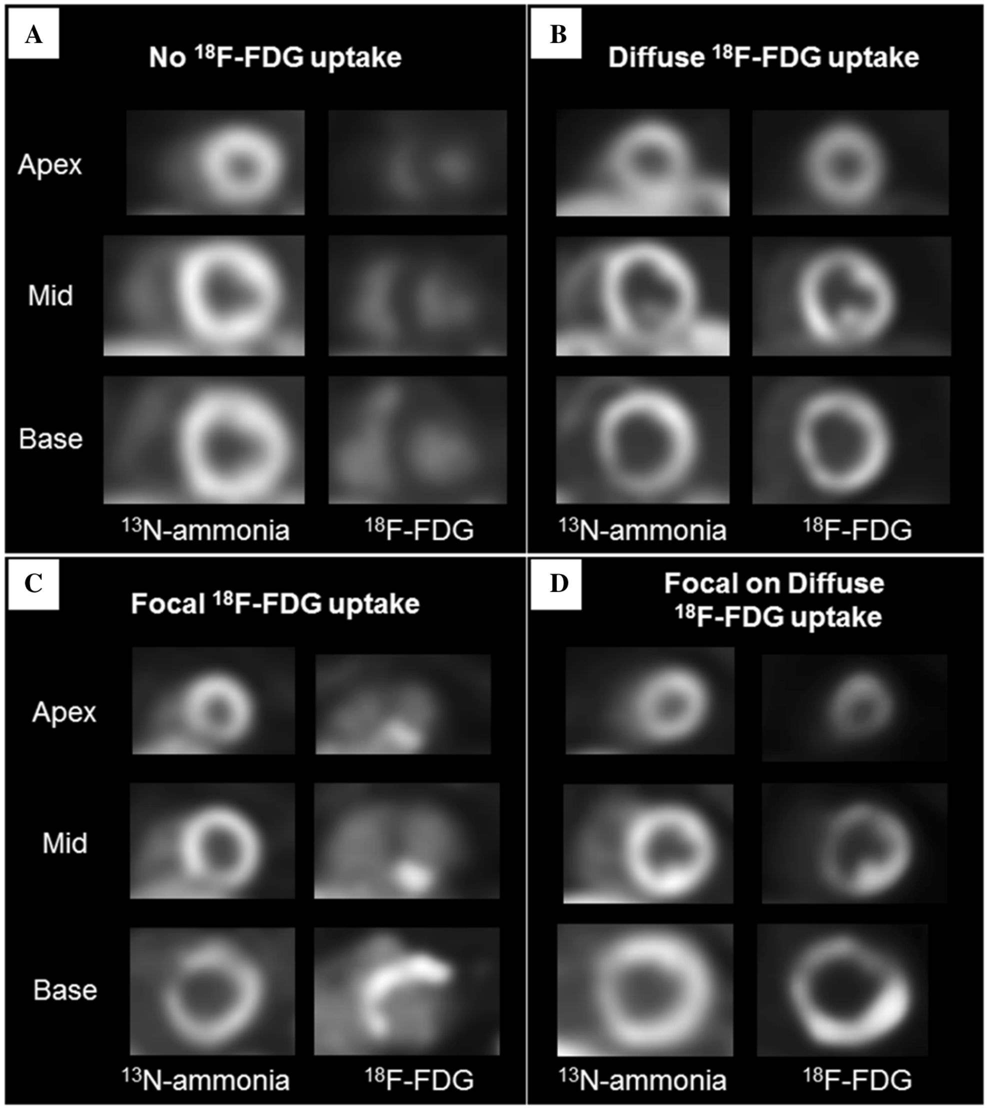


**Figure 1.** Patterns of myocardial $^{18}$F-FDG uptake on cardiac PET. Patterns of myocardial 18-fluorodeoxyglucose (FDG) uptake were interpreted per established guidelines as follows: (**A**) No $^{18}$F-FDG uptake, (**B**) diffuse myocardial $^{18}$F-FDG uptake, (**C**) focal $^{18}$F-FDG uptake, and (**D**) focal on diffuse $^{18}$F-FDG. Patients presented in panels (**A**) and (**C**) were considered to have appropriate suppression of physiologic myocardial $^{18}$F-FDG uptake while (**B**) had suboptimal suppression of myocardial $^{18}$F-FDG uptake. Patients in panel (**D**) had either appropriate or suboptimal suppression of myocardial $^{18}$F-FDG uptake based on discretion of the cardiac imager (see Methods).

meals the day prior to the $^{18}$F-FDG PET study, and fast for at least 15 hours after the meals before the PET study. Detailed examples of HFLC meals and permissible vs undesirable foods were provided. Patients were also instructed not to exercise for 24 hours prior to the PET examination. An alternative option to the combined HFLC meals and fasting was an 18-hour fast, but this approach was discouraged by nursing staff when the patients were called 48 hours prior to testing. On the day of the study, nursing/technical staff ensured that patients have strictly followed the recommended instructions and reviewed the food diary questionnaire. Compliance with the new preparation protocol was ensured by a combination of detailed written instructions (Appendix 1), a phone call from nursing staff 48 hours before the PET study, and a food diary questionnaire (Appendix 2), which was reviewed by healthcare providers at the time of the study. Both outpatients and inpatients were included in the study and the same dietary instructions were provided to both. In the case of inpatients, we worked closely with the dietetics team and nursing staff to ensure dietary compliance. Based on review of the food diary questionnaire, patients were categorized as fully compliant, partially compliant, or non-compliant. Non-compliant patients were not scanned and were instructed to return after following the protocol. Partial compliance was defined as (1) limited carbohydrate consumption (1-2 carbohydrate containing options described in Appendix 2), (2) a last food intake past 5 p.m. (but not past 7 p.m.) the day prior to PET scan, or (3) exercise the day prior to PET scan. Non-compliance was defined as more than 3 carbohydrate items listed in Appendix 2 or late food intake (after 7 p.m. the day prior to PET scan).

## Data Collection

Data were retrospectively collected, prospectively analyzed, and included all consecutive PET scans performed at our institution for the assessment of CS between March 2010 and September 2017. In patients who had multiple studies either before or after application of the new protocol, only the first of the studies before August 2016 and the first of the studies after August 2016 were included in the analysis. This was done to avoid data duplication and patient over-representation in the study sample. Other clinical variables were obtained via manual review of the electronic medical record.

## PET Sarcoidosis Protocol

PET scans were performed using the GE Advance PET camera (GE Medical Systems, Milwaukee, WI, USA) between March 2010 and January 2016. The GE Discovery PET/CT camera (GE Medical Systems, Milwaukee, WI, USA) was used for all tests performed starting in February 2016 through September 2017. A 10-minute transmission scan utilizing $^{68}$Germanium rod sources was used for attenuation correction with the GE Advance camera. Computed tomography was used for attenuation correction in scans performed with the GE Discovery camera (helical scanning, slice thickness 3.75 mm, interval 3.27 mm, 120 kVp with arms elevated (default) or 140 kVp with arms along the side). Initial images included myocardial perfusion assessment using $N^{13}$ ammonia (10-20 mCi) administered via intravenous injection. Following acquisition of perfusion images, inflammation was assessed using $^{18}$F-FDG (15-20 mCi) administered via intravenous injection. The resting $^{18}$F-FDG scan was performed after a period of 60 minutes following $^{18}$F-FDG administration to allow for $^{18}$F-FDG uptake. With the GE Discovery PET/CT camera, image acquisition was performed in 3D for 10 minutes. PET/CT fusion images were reviewed for accurate co-registration to ensure accuracy of attenuation correction. Gated perfusion as well as static perfusion and $^{18}$F-FDG series were transferred to an in-house developed nuclear cardiology viewing software[10] as well as a nuclear medicine dedicated software (MIM Software Inc, Cleveland, Ohio). Myocardial perfusion and $^{18}$F-FDG images were displayed in 3 orthogonal planes (short axis, vertical long axis, and horizontal long axis). Myocardial perfusion and $^{18}$F-FDG uptake were assessed in each of the standard 17 myocardial segments as described previously.[11] Attenuation corrected as well as non-corrected images were also reviewed using a general nuclear medicine hybrid display software (MIM Software Inc., Cleveland, OH, USA).

## Image Interpretation

PET images of patients who underwent the study using the old preparation protocol (group 1) vs the new preparation protocol (group 2) were evaluated for suppression of physiologic myocardial $^{18}$F-FDG uptake. All studies were interpreted by consensus of two staff cardiologists with specialized training in advanced nuclear cardiac imaging. Interpretation of myocardial $^{18}$F-FDG uptake was performed as per the 2017 SNMMI and ASNC guidelines as follows: 1) No $^{18}$F-FDG uptake, 2) Focal $^{18}$F-FDG uptake, 3) Diffuse $^{18}$F-FDG uptake, and 4) Focal on diffuse $^{18}$F-FDG uptake (Figure 1).[3] Patients with focal $^{18}$F-FDG uptake or no $^{18}$F-FDG uptake were considered to have complete suppression of physiologic $^{18}$F-FDG uptake. Patients with diffuse $^{18}$F-FDG uptake were considered to have suboptimal suppression of physiologic $^{18}$F-FDG uptake. Patients with focal on diffuse myocardial $^{18}$F-FDG uptake were reviewed by HJ and if 4 or more myocardial segments had normal perfusion without $^{18}$F-FDG uptake, physiologic $^{18}$F-FDG suppression was considered adequate. We based this on the assumption that physiologic myocardial $^{18}$F-FDG uptake is uniform and it would be very unlikely to have differential suppression of myocardial $^{18}$F-FDG uptake between various segments. Isolated basal lateral $^{18}$F-FDG uptake has been reported to be a normal variant in the literature and was not considered to represent inadequate $^{18}$F-FDG suppression.

## Statistical Analysis

Continuous variables were expressed as means (standard deviation) and compared using student's $t$ test. Categorical variables were expressed as numbers (percentage) and compared using the Chi-square test. Comparison of matched pairs was performed using the McNemar's test. A two-tailed $P$ value of $< .05$ was used to determine statistical significance. All analyses were performed using JMP software version 9.0 (SAS institute, Cary, NC, USA).

# RESULTS

Of the 366 patients that underwent sarcoidosis PET scans, 134 had the old preparation protocol (group 1) and 232 had the new preparation protocol (group 2). Patient characteristics are summarized in Table 2. There were no statistically significant differences in age, sex, body mass index, diabetes mellitus, coronary artery disease, or left ventricular ejection fraction between the two groups. Glucose levels at the time of PET scan and were $94 \pm 24$ mg·dL$^{-1}$ (group 2) and $101 \pm 21$ mg·dL$^{-1}$ (group 1) ($P = .04$). Inpatients represented 5% of the total patient population and were overrepresented in group 1 ($P = .03$). $^{18}$F-FDG myocardial suppression was noted in 78% of PET scans in group 1 compared to 91% of PET scans in group 2 ($P < .001$, Table 2). Among patients in group 1, ''diffuse'' myocardial $^{18}$F-FDG uptake (indicative of suboptimal physiologic $^{18}$F-FDG

**Table 2.** Patient characteristics and PET findings

| | New protocol (n = 232) | Old protocol (n = 134) | *P* |
|---|---|---|---|
| Age, years | 57±12 | 56±12 | .29 |
| Male, n (%) | 144 (62%) | 80 (60%) | .70 |
| Body mass index ($kg \cdot m^{-2}$) | 31±7 | 30±7 | .34 |
| Diabetes, n (%) | 30 (13%) | 19 (14%) | .74 |
| Glucose at time of scanning ($mg \cdot dL^{-1}$) | 94±24 | 101±21 | .04 |
| Coronary artery disease, n (%) | 16 (7%) | 13 (10%) | .33 |
| Perfusion defects associated with FDG uptake | 119 (51%) | 79 (59%) | .13 |
| Left ventricular ejection fraction (%) | 46±14 | 45±15 | .55 |
| Inpatient (%) | 7 (3%) | 11 (8%) | .03 |
| FDG uptake pattern | | | |
| None, n (%) | 128 (55%) | 43 (32%) | < .001 |
| Focal, n (%) | 61 (26%) | 55 (41%) | .003 |
| Focal on Diffuse, n (%) | 38 (16%) | 20 (15%) | .71 |
| Diffuse, n (%) | 5 (2%) | 16 (12%) | < .001 |
| Image interpretation | | | |
| Complete suppression of myocardial $^{18}$F-FDG uptake, n (%) | 212 (91%)* | 105 (78%) | < .001 |
| I solated basal lateral FDG uptake (normal variant) | 5 (2%) | 3 (2%) | .96 |

*Includes both compliant and partially compliant patients. Note that the total number of patients interpreted as complete suppression of myocardial $^{18}$F-FDG uptake includes all patterns interpreted 'focal' or 'none' and selected patterns interpreted as 'focal on diffuse' based on discretion of the cardiac imager

suppression) was noted in 12% of these studies compared to only 2% of studies in group 2, ($P < .001$). In group 2, prolonged fasting (at least 18 hours) was the preparation of choice in 13 patients (6%) and was associated with adequate $^{18}$F-FDG suppression in 11 patients (85%).

Regarding the new preparation protocol (group 2), complete compliance and partial compliance were noted in 70% and 30% of the patients, respectively. No major differences were noted in compliance rates between males (71%) vs females (68%) ($P = .63$). Exercise prior to PET scanning was the cause of partial compliance in 2% of patients. Partial compliance in group 2 was associated with adequate $^{18}$F-FDG suppression in 88% of patients. Patients who had suboptimal physiologic suppression of $^{18}$F-FDG uptake in group 2 had compliance rates of 50% (10 out of 20 patients). Patients who had partial compliance had physiologic $^{18}$F-FDG suppression in 88% of cases and patients who had complete compliance had physiologic $^{18}$F-FDG suppression in 93% of cases ($P = .31$).

There were 47 patients who underwent 2 PET scans in the study period; one utilizing the old preparation protocol and the later scan utilizing the new preparation protocol. In these patients, physiologic myocardial $^{18}$F-FDG suppression was achieved in 85% using the old protocol compared to 96% using the new protocol, albeit this difference was not statistically significant ($P = .18$, likely due to lack of statistical power). Of the 47 patients, 7 patients had inadequate $^{18}$F-FDG suppression that changed to adequate $^{18}$F-FDG suppression, 2 patients had adequate $^{18}$F-FDG suppression that changed to inadequate $^{18}$F-FDG suppression, and 38 patients had adequate $^{18}$F-FDG suppression before and after the protocol changed.

## DISCUSSION

The present study shows that implementation of a structured and detail-oriented patient preparation protocol in line with the SNMMI/ASNC expert consensus document was successful in suppressing physiologic myocardial $^{18}$F-FDG uptake in most patients undergoing cardiac PET for CS. To the best of our knowledge, our study is the largest in the literature to assess appropriate suppression of myocardial $^{18}$F-FDG uptake using a structured patient preparation protocol. The frequency of diffuse myocardial $^{18}$F-FDG uptake, associated with false positives, decreased 6-fold using the new protocol and complete suppression of physiologic myocardial $^{18}$F-FDG uptake was achieved in 91% of patients appropriately following the new protocol compared to 78% using the old protocol.

The optimal preparation for sarcoidosis PET scan is not well established. Different strategies to suppress physiologic myocardial $^{18}$F-FDG uptake have included prolonged fasting, dietary manipulation, intravenous heparin, or a combination of the above methods. Prolonged fasting for at least 12-18 hours has been successful in suppressing physiologic $^{18}$F-FDG uptake. However, it is laborious and is associated with decreased patient compliance.[8] Dietary manipulation is the most common preparation method due to its efficacy and patient tolerability. It most commonly includes a low-carbohydrate diet or a low-carbohydrate/high-fat diet, often in combination with fasting. The exact amount of fat or carbohydrate intake has not been standardized although more than 35 grams of fat and less than 5 g of carbohydrates were suggested in a prior study.[12] Several studies have trialed a high-fat meal or beverage in the last hours prior to the scan without significant benefit.[13–15] Lastly, low-dose intravenous heparin administration increases lipolysis and plasma free fatty acid levels in healthy individuals, and has been utilized, alone or in combination with dietary manipulation, to suppress $^{18}$F-FDG uptake, with variable results.[7,16]

Prior research shows great variability in the adequacy of physiologic myocardial $^{18}$F-FDG uptake suppression. In a recent review of 31 studies by Osborne and colleagues, success rates ranged between 10 and 100%.[8] Studies with unrestricted diet and short fasting periods (< 12 hours) tended to be less successful achieving proper suppression of myocardial $^{18}$F-FDG uptake (10-60%). However, studies that implemented prolonged fasting (> 12 hours), with or without dietary manipulation prior to the fasting period yielded the highest success rates (60-100%). Manabe et al reported a 0% diffuse uptake rate in 24 patients who underwent preparation with a low-carbohydrate diet, an 18-hour fast, as well as intravenous heparin.[6] However, the small patient sample size does not allow for definitive conclusions. Coulden and colleagues reported a 98% success rate with a low-carbohydrate diet ''Atkins diet'' prior to >8 hours of fast in 94 patients.[17] However, Coulden et al defined successful suppression of myocardial $^{18}$F-FDG uptake as myocardial maximum standard uptake values < 3.6 without describing the pattern of myocardial $^{18}$F-FDG uptake. Of note, a large proportion of their intervention group (n = 26, 22%) were non-compliant with the recommended dietary instructions and were excluded from the study. In the largest currently available study by Blankstein and colleagues, success rate was 87% in 118 patients with applications of a high-fat, no-carbohydrate diet for two meals with a 4-hour fast.[18] Similar results and a 90% success rate were reported by Harisankar et al in 60 patients who had a similar preparation.[4] Lastly, a high-fat, low-carbohydrate combination diet for > 24 hours with heparin achieved an 84% success rate in 89 patients as reported by Nensa et al [19]

Based on prior literature and anecdotal experience, our institution modified the patient preparation protocol for cardiac sarcoidosis in August 2016. We identified that the major culprit for inadequate $^{18}$F-FDG suppression was patient non-compliance. As such, the new protocol aimed to enhance timely patient education and re-enforcement. Providing a list of dietary options is presumably superior to patient-driven options. Moreover, having the patients log their food in the preparation timeframe likely increases food awareness and overall compliance. A prolonged fasting option may be suitable for select patients (vegetarian/vegan patients or patients with difficulty logging their food items). Since the evidence for benefit of high-fat meals in the 12 hours prior to PET scan is lacking, those interventions were eliminated from the new preparation protocol. It is possible that eliminating the HFLC morning meal on the day of the scan also improves PET imaging quality, since it eliminates the possibility of inadvertent carbohydrate intake close to the time of testing. Exercise prior to scanning has been postulated to result in an increase in skeletal muscle and myocardial FDG uptake via a norepinephrine-mediated mechanism. Accordingly, patients were instructed not to exercise for 24 hours prior to PET scan although the contribution of this intervention was hard to quantify (only two patients reported exercise with the new protocol and were termed partially compliant). Lastly, heparin administration prior to the scan was not used given the inconsistent evidence to support its use as well as institutional constraints regarding heparin use in the outpatient setting. It should be noted that although the new preparation protocol was designed to promote compliance, complete dietary adherence is likely difficult to achieve and 30% of the group 2 patients had only partial compliance.

Our study demonstrated a success rate of 91% in suppressing physiologic myocardial uptake. It is noteworthy that 50% of cases with suboptimal physiologic myocardial $^{18}$F-FDG suppression in patients using the new preparation protocol were only partially compliant with the provided instructions, which could possibly underestimate the protocol's true success rate when the dietary instructions are followed completely. Conceivably, our study's protocol could be implemented at other tertiary centers with high volumes of CS studies to improve myocardial suppression of physiologic $^{18}$F-FDG uptake. This can improve the specificity of positive myocardial $^{18}$F-FDG uptake which has significant diagnostic and therapeutic implications in patients with CS. Additionally, it may also decrease cost and patient radiation dose related to repeat testing.

Several important limitations warrant discussion: (1) The present study was performed at a single tertiary academic institution; therefore, care should be exercised when extrapolating our results to other centers. (2) By study design, our PET image analysis used in this study was semi-quantitative. Inter-observer variability in image interpretation and classification is possible and could be subjective to some degree.[20] However, error from misclassification would be random rather than systematic and having two reviewers for each study minimizes the odds of misinterpretation or misclassification. (3) We did not quantify fat and carbohydrate amounts consumed in our study since this quantification is difficult. We presumed that a patient strictly adhering to the suggested meals would have consumed < 3 grams of carbohydrate (amount suggested by SNMMI/ASNC consensus document). (4) Patient over-representation bias from including sequential PET scans in the study could potentially skew results in favor of the new preparation protocol, particularly since patients requiring repeat follow-up testing can learn what dietary habits are most appropriate and effectively suppress physiologic $^{18}$F-FDG uptake in the subsequent scans. However, only 7 of the 47 patients that were included in both groups 1 and 2 in our study had a change from inadequate to adequate physiologic suppression. (5) We did not assess the clinical implications of CS presentation and treatment on PET myocardial $^{18}$F-FDG imaging findings, as this was beyond the scope of this study.

In conclusion, we describe an efficacious structured patient preparation protocol that included clear communication of dietary instructions between healthcare providers and patients, in agreement with the SNMMI/ASNC expert consensus document. This protocol was highly successful in achieving complete suppression of physiologic myocardial $^{18}$F-FDG uptake and should be strongly considered to promote patient adherence and improve PET image quality.

## NEW KNOWLEDGE GAINED

- A structured protocol of combined high-fat low-carbohydrate meals and prolonged fasting with compliance reinforcement and detailed patient instructions as recommended by the joint SNMMI/ASNC expert consensus document can significantly suppress physiologic $^{18}$F-FDG uptake in positron emission tomography for cardiac sarcoidosis.
- Partial compliance with a strict protocol can result from inadvertent carbohydrate consumption, decreased time interval of prolonged fasting, and exercise, is only achieved in 70% patients, and could potentially result in failure to suppress physiologic myocardial $^{18}$F-FDG uptake.

### Acknowledgements

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### Disclosure

*All authors do not have any relationships to disclose.*

## APPENDIX 1. WRITTEN INSTRUCTIONS PROVIDED TO PATIENTS UNDERGOING SARCOID PET SCAN ACCORDING TO THE NEW PREPARATION PROTOCOL

**For 24 hours before the test:**

- Do not exercise.

**You have two options for eating and drinking before your test.**

**The preferred option (Option 1):**

**Eating and drinking:**

Keep a log of everything you eat the day before your scan.

**Before 5 pm the day before your test:**

- Eat a diet high in fat and protein with no carbohydrates. See the suggested diet.
- Do not eat after 5 p.m. the day before your scan.

**For breakfast, lunch, and dinner the day before your scan:** Choose one of the following for each meal:

- 3 to 5 fatty sausage links fried in oil or butter.
- 2 hamburger patties fried in oil or butter.
- 3 to 5 bacon strips.

- Fried chicken or fatty fish fried in oil or butter. No breading.
- 8 oz. fatty steak fried in oil or butter.
- 3 eggs fried in oil or butter (no milk or cheese).

Drink only water or clear liquids (tea, coffee without sugar, no added cream or milk).

**Do not eat:**

- Vegetables, beans, nuts, fruits, juices, bread, grains, pasta, or any baked good.
- Sweetened, grilled, or cured meats with additives that contain carbohydrates.
- All dairy products, except butter.
- Sweets, candy, gum, lozenges, and sugar.
- Alcoholic beverages, sodas, that contain sugar, fruits juice, and sports drinks.
- Mayonnaise, ketchup, tartar sauce, mustard, and other condiments.

**The acceptable option (Option 2):**
**Eating and Drinking:**
Keep a log of everything you eat the day before your scan.
**18 hours before the day of your test:**
Do not eat anything for 18 hours before your appointment time. You may continue to drink plain water only.
**One hour before your test:** Stop drinking water.

## APPENDIX 2. PATIENT QUESTIONNAIRE FOR CARDIAC PET IMAGING FOR SARCOIDOSIS

Patient Name: ____________________ Medical Record Number #: ______________

**Did you exercise in the last 24 hours?**

__ Yes __ No **What time did you eat last? ______**

**Did you follow the dietary instructions in the patient guide?**

__ Yes 100% __ Yes, mostly __ No

**I am unable to eat any of the foods in the instructions and I have been fasting since yesterday (enter time) ____, or today (enter time) ____ .**

**For those who followed the diet instructions, what did you eat for breakfast yesterday? Record serving sizes.**

______________________________________________________________________

______________________________________________________________________

Did you eat any of the following items for breakfast? __ Yes __ No

If yes, mark the items you consumed for breakfast.

- Vegetables, beans, nuts, fruits and juices
- Bread, grain, rice, pasta, all baked goods
- Sweetened, grilled or cured meats or meat with carbohydrate-containing additives (some sausages, ham, sweetened bacon)
- Dairy products aside from butter (milk, cheese, etc)
- Candy, gum, lozenges and sugar
- Alcoholic beverages, soda and sports drinks
- Mayonnaise, ketchup, tartar sauce, mustard and other condiments.

**For those who followed the diet instructions, what did you eat for lunch yesterday? Record serving sizes.**

______________________________________________________________

______________________________________________________________

Did you eat any of the following items for lunch? __ Yes __ No

If yes, mark the items you consumed for lunch.

- Vegetables, beans, nuts, fruits and juices
- Bread, grain, rice, pasta, all baked goods
- Sweetened, grilled or cured meats or meat with carbohydrate-containing additives (some sausages, ham, sweetened bacon)
- Dairy products aside from butter (milk, cheese, etc)

- ☐ Candy, gum, lozenges and sugar
- ☐ Alcoholic beverages, soda and sports drinks
- ☐ Mayonnaise, ketchup, tartar sauce, mustard and other condiments.

**For those who followed the diet instructions, what time did you eat dinner yesterday? ____ pm.**

**What did you eat for dinner? Record serving sizes.**

______________________________________________

______________________________________________

Did you eat any of the following items for dinner? __ Yes __ No

If yes, mark the items you consumed for dinner.

- ☐ Vegetables, beans, nuts, fruits and juices
- ☐ Bread, grain, rice, pasta, all baked goods
- ☐ Sweetened, grilled or cured meats or meat with carbohydrate-containing additives (some sausages, ham, sweetened bacon)
- ☐ Dairy products aside from butter (milk, cheese, etc)
- ☐ Candy, gum, lozenges and sugar
- ☐ Alcoholic beverages, soda and sports drinks
- ☐ Mayonnaise, ketchup, tartar sauce, mustard and other condiments.

**For those who followed the diet instruction, did you eat anything after your dinner? __ Yes __ No __ What time did you eat if you ate after dinner? __ pm**

## References

1. Patel MR, Cawley PJ, Heitner JF, Klem I, Parker MA, Jaroudi WA, Meine TJ, White JB, Elliott MD, Kim HW, Judd RM, Kim RJ. Detection of myocardial damage in patients with sarcoidosis. Circulation 2009;120:1969-77.
2. Silverman KJ, Hutchins GM, Bulkley BH. Cardiac sarcoid: A clinicopathologic study of 84 unselected patients with systemic sarcoidosis. Circulation 1978;58:1204-11.
3. Chareonthaitawee P, Beanlands RS, Chen W, Dorbala S, Miller EJ, Murthy VL, Birnie DH, Chen ES, Cooper LT, Tung RH, White ES, Borges-Neto S, Di Carli MF, Gropler RJ, Ruddy TD, Schindler TH, Blankstein R. Joint snmmi-asnc expert consensus document on the role of 18F-FDG PET/CT in cardiac sarcoid detection and therapy monitoring. J Nucl Cardiol 2017

4. Harisankar CN, Mittal BR, Agrawal KL, Abrar ML, Bhattacharya A. Utility of high fat and low carbohydrate diet in suppressing myocardial FDG uptake. J Nucl Cardiol 2011;18:926-36.
5. Bois JP, Chareonthaitawee P. Continuing evolution in preparation protocols for 18FDG pet assessment of inflammatory or malignant myocardial disease. J Nucl Cardiol 2017;24:989-92.
6. Manabe O, Yoshinaga K, Ohira H, Masuda A, Sato T, Tsujino I, Yamada A, Oyama-Manabe N, Hirata K, Nishimura M, Tamaki N. The effects of 18-h fasting with low-carbohydrate diet preparation on suppressed physiological myocardial (18)f-fluorodeoxyglucose (FDG) uptake and possible minimal effects of unfractionated heparin use in patients with suspected cardiac involvement sarcoidosis. J Nucl Cardiol 2016;23:244-52.
7. Masuda A, Naya M, Manabe O, Magota K, Yoshinaga K, Tsutsui H, Tamaki N. Administration of unfractionated heparin with prolonged fasting could reduce physiological 18f-fluorodeoxyglucose uptake in the heart. Acta Radiol 2016;57:661-8.
8. Osborne MT, Hulten EA, Murthy VL, Skali H, Taqueti VR, Dorbala S, DiCarli MF, Blankstein R. Patient preparation for cardiac fluorine-18 fluorodeoxyglucose positron emission tomography imaging of inflammation. J Nucl Cardiol 2017;24:86-99.
9. Bois JP, Chareonthaitawee P. Patient page-sarcoidosis imaging. J Nucl Cardiol 2017
10. Aggarwal NR, Drozdova A, Askew JW 3rd, Kemp BJ, Chareonthaitawee P. Feasibility and diagnostic accuracy of exercise treadmill nitrogen-13 ammonia pet myocardial perfusion imaging of obese patients. J Nucl Cardiol 2015;22:1273-80.
11. Cerqueira MD, Weissman NJ, Dilsizian V, Jacobs AK, Kaul S, Laskey WK, Pennell DJ, Rumberger JA, Ryan T, Verani MS. American Heart Association Writing Group on Myocardial S, Registration for Cardiac I. Standardized myocardial segmentation and nomenclature for tomographic imaging of the heart. A statement for healthcare professionals from the cardiac imaging committee of the council on clinical cardiology of the American Heart Association. Circulation 2002;105:539-42.
12. Demeure F, Hanin FX, Bol A, Vincent MF, Pouleur AC, Gerber B, Pasquet A, Jamar F, Vanoverschelde JL, Vancraeynest D. A randomized trial on the optimization of 18f-fdg myocardial uptake suppression: Implications for vulnerable coronary plaque imaging. J Nucl Med 2014;55:1629-35.
13. Cheng VY, Slomka PJ, Ahlen M, Thomson LE, Waxman AD, Berman DS. Impact of carbohydrate restriction with and without fatty acid loading on myocardial 18f-fdg uptake during pet: A randomized controlled trial. J Nucl Cardiol 2010;17:286-91.
14. Kobayashi Y, Kumita S, Fukushima Y, Ishihara K, Suda M, Sakurai M. Significant suppression of myocardial (18)f-fluorodeoxyglucose uptake using 24-h carbohydrate restriction and a low-carbohydrate, high-fat diet. J Cardiol 2013;62:314-9.
15. Wykrzykowska J, Lehman S, Williams G, Parker JA, Palmer MR, Varkey S, Kolodny G, Laham R. Imaging of inflamed and vulnerable plaque in coronary arteries with 18F-FDG PET/CT in patients with suppression of myocardial uptake using a low-carbohydrate, high-fat preparation. J Nucl Med 2009;50:563-8.
16. Gormsen LC, Christensen NL, Bendstrup E, Tolbod LP, Nielsen SS. Complete somatostatin-induced insulin suppression combined with heparin loading does not significantly suppress myocardial 18f-fdg uptake in patients with suspected cardiac sarcoidosis. J Nucl Cardiol 2013;20:1108-15.
17. Coulden R, Chung P, Sonnex E, Ibrahim Q, Maguire C, Abele J. Suppression of myocardial 18f-fdg uptake with a preparatory ''atkins-style'' low-carbohydrate diet. Eur Radiol 2012;22:2221-8.
18. Blankstein R, Osborne M, Naya M, Waller A, Kim CK, Murthy VL, Kazemian P, Kwong RY, Tokuda M, Skali H, Padera R, Hainer J, Stevenson WG, Dorbala S, Di Carli MF. Cardiac positron emission tomography enhances prognostic assessments of patients with suspected cardiac sarcoidosis. J Am Coll Cardiol 2014;63:329-36.
19. Nensa F, Tezgah E, Schweins K, Goebel J, Heusch P, Nassenstein K, Schlosser T, Poeppel TD. Evaluation of a low-carbohydrate diet-based preparation protocol without fasting for cardiac pet/mr imaging. J Nucl Cardiol 2017;24:980-8.
20. Ohira H, Ardle BM, deKemp RA, Nery P, Juneau D, Renaud JM, Klein R, Clarkin O, MacDonald K, Leung E, Nair G, Beanlands R, Birnie D. Inter- and intraobserver agreement of (18)F-FDG PET/CT image interpretation in patients referred for assessment of cardiac sarcoidosis. J Nucl Med 2017;58:1324-9.