Variances of dietary preparation for suppression of physiological ^{18}F-FDG myocardial uptake in the presence of cardiac sarcoidosis: A systematic review

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Background. **^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography (PET) is used in the diagnosis and management of patients with cardiac sarcoidosis (CS). Various preparation protocols have been proposed to minimise myocardial ^{18}F-FDG uptake and improve scan readability. The aim of this systematic review was to identify the optimal dietary prescription for suppression of physiological ^{18}F-FDG myocardial uptake to enhance clinical diagnosis of CS.**

Methods and Results. **MEDLINE and PubMed databases identified 13 studies meeting inclusion criteria for review. Articles were assessed using the Australian National Health and Medical Research Council levels of evidence and categorised as sarcoidosis (human) or non-sarcoidosis (human, animal). Visual uptake scales (qualitative) and/or standardised uptake values (SUV) (quantitative) were used in all the studies reviewed. Nine of 11 human studies showed statistically significant improvements in PET scan interpretation with carbohydrate-restricted diets compared with fasting only, and when carbohydrates were restricted for a longer period of time. Two animal studies showed statistically significant improvements following very low carbohydrate diet preparation (0.01% and 0.4% carbohydrate diets) compared with higher carbohydrate diets.**

Conclusions. **Variation in measures used, dietary prescriptions, fasting times, species and study quality makes result comparison and applicability difficult. Definitive dietary recommendations are not possible based on current evidence. (J Nucl Cardiol 2020;27:481–9.)**

Key Words: Sarcoid heart disease • CT • PET • Molecular imaging • Molecular imaging agents • ^{18}F-FDG • Sarcoidosis • Fasting • Low-carbohydrate diet

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INTRODUCTION

The diagnosis of cardiac sarcoidosis (CS) can be difficult to establish owing to a lack of robust diagnostic methods. Recently, ^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography (PET) has emerged as a useful, non-invasive tool in the management of patients with CS. The suppression of physiological myocardial ^{18}F-FDG uptake assists clinicians in the interpretation of PET scan results by enhancing scan clarity and improving readability.[1] Optimal approaches to minimize this physiological uptake remain controversial with numerous preparatory guidelines proposed, including the use of pharmacological interventions such as unfractionated heparin and calcium channel blockers.[1,2] Of particular interest, an increasing number of patient preparation protocols for ^{18}F-FDG PET involve extended fasting and carbohydrate restriction, however, significant variation in dietary preparations have been reported in the literature. The aim of this systematic review was to identify the optimal dietary prescription for suppression of physiological ^{18}F-FDG myocardial uptake to enhance clinical diagnosis of CS.

METHODS

Search Strategy

Articles were retrieved via a comprehensive literature search using MEDLINE and PubMed databases without date restrictions. Two search strategies were conducted using search terms selected from known articles relevant to the subject. *Search 1* included: Fluorodeoxyglucose F18; Myocardium OR Cardiac; diet OR carb* OR fat; sarcoidosis. *Search 2* included: Fluorodeoxyglucose F18; Myocardium OR Cardiac; diet OR carb* OR fat. Articles published prior to April 2017 were retrieved. No limitations were placed on language or subject group.

Selection Criteria

As illustrated in Figure 1, the abstracts of potentially relevant articles were retrieved (*Search 1*, $n = 27$; *Search 2*, $n = 238$). Articles were excluded if the title or abstract did not address the study aim. Following initial screening and after removing duplicates, 11 articles for *Search 1* and 21 studies for *Search 2* were retrieved for detailed evaluation. Included articles compared myocardial uptake of ^{18}F-FDG following the prescription of two or more different dietary preparations. Studies that compared fasting time with dietary preparations were also included, however, studies comparing fasting times alone were excluded. Upon further review, four and nine articles met inclusion criteria for *Search 1* and *Search 2* respectively.

Results were considered statistically significant with a probability value of < 0.05. Clinically significant results, based on nuclear medicine physicians' review, were reported as documented by the published papers. Articles were graded using the Australian National Health and Medical Research Council (NHMRC) levels of evidence.[3] The NHMRC levels of evidence categorizes published studies from the greatest to least strength of evidence, that is systematic review of level II studies (Level I), to randomized control trial (Level II),

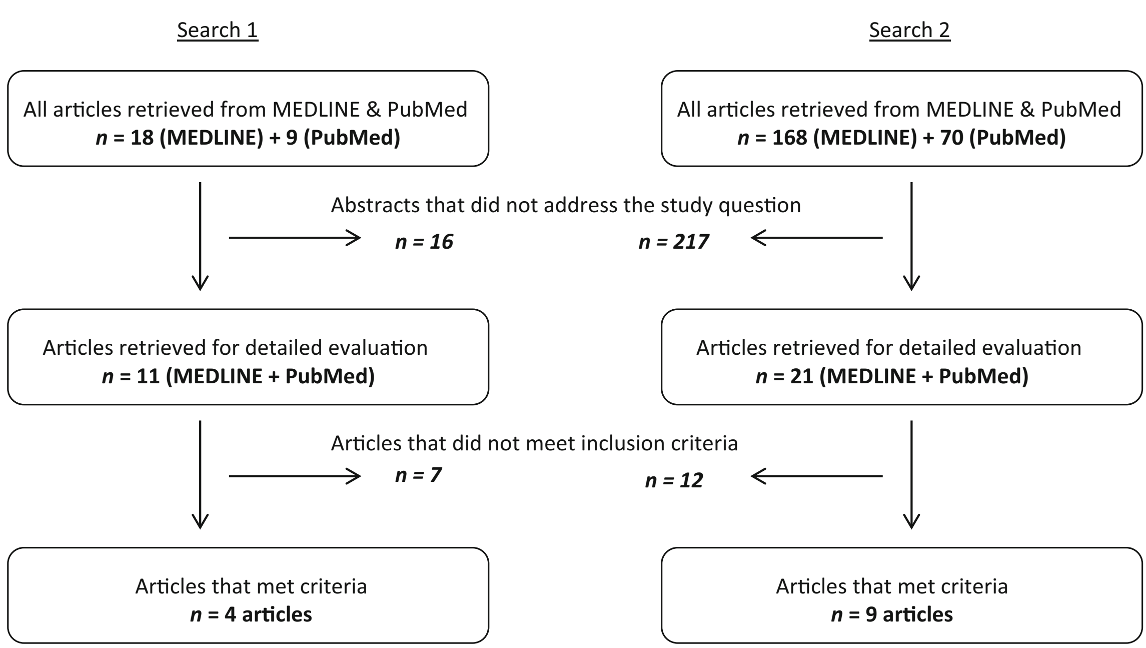

Figure 1. Flow diagram of articles retrieved for review from two databases.

followed by cohort or case control study (Level III), and lastly case series (Level IV).

RESULTS

As described in Table 1, two measures were primarily used to establish an improvement in the interpretation of ^{18}F-FDG PET images following prescribed dietary preparations. Visual uptake scales (qualitative) and/or Standardized Uptake Values (SUV) (quantitative) were used in all the studies reviewed.

Almost all (10 of the 11) human studies reviewed reported statistically significant results, of these: four provided qualitative diet details only[4–7]; three provided quantitative diet details only[8–10]; two provided both qualitative and quantitative diet details [2,11;] and one provided neither qualitative nor quantitative diet details.[1] When quantitative details were provided, the amount of carbohydrate prescribed greatly varied, ranging from < 3 g [9] up to approximately 45 g (if all three dairy choices consumed were milk or yogurt as allowed in the dietary protocol)[11] of carbohydrates the day prior to the scan. The diet preparation protocols described qualitatively by the reviewed studies also varied greatly.

As outlined in Table 1, nine of the 11 human studies showed a statistically significant improvement in PET scan interpretation following a carbohydrate-restricted (with or without 'high fat') dietary preparation compared with fasting only.[1,2,5–11] A carbohydrate-restriction with a high fat supplement drink (Benecalorie®) 60-70 minutes prior to the scan, did not improve scan interpretation compared with carbohydrate restriction alone.[8] Fasting times were consistent between the study groups in two of these nine studies.[9,11] In the remaining studies, the fasting only group and the dietary intervention group/s fasted for differing lengths of time before their scans. The largest variance in fasting time was a ≥ 6 hour fast for the fasting only group and a ≥ 18 hour fast for the dietary intervention group.[2] One human study[4] showed significantly improved results after the same dietary preparation (described as high fat, high protein, very low carbohydrate) was followed for a longer period of time (72 hours of diet restriction compared with < 24 hours of diet restriction).

Two animal studies conducted with mice and rats were identified in this review. These studies enabled manipulation of animal feed and therefore provided highly specific quantitative details regarding the dietary preparation.[12,13] Both studies reported statistically significant results, which, in accord with the human studies reviewed, indicated a reduced carbohydrate intake prior to cardiac PET leads to improved ^{18}F-FDG uptake suppression. One study found that both a 'sunflower seed' diet (18% carbohydrate, 55% fat) and a 'ketogenic' diet (0.4% carbohydrate, 90% fat) resulted in reduced physiological cardiac uptake compared to a 'regular' diet (72.4% carbohydrate, 8.4% fat).[12] A statistically significant improvement was found with the 'ketogenic' diet compared to the 'sunflower seed diet' when using the visual uptake scale, however this comparison was not statistically significant when using the SUV_{max} measurement. In the other animal study, a 'low carbohydrate' diet (0.01% carbohydrate, 90% fat) produced better scan results than both an 'intermediate carbohydrate' diet (52% carbohydrate, 28% fat) and a 'high carbohydrate' diet (78% carbohydrate, 2% fat).[13] This difference reached statistical significance using the SUV_{max} measurement. No statistical significance was found between the 'intermediate carbohydrate' and 'high carbohydrate' diets.

Two of the 13 studies reviewed were of level II evidence[8,13] while the remainder were of level III (n = 9)[1,2,4–7,9,11,14] and level IV (n = 2)[10,12] evidence (see Table 1). The low grading of evidence for most of these studies was due to the predominant use of cohort or case series study designs.

DISCUSSION

The results of this review highlight significant variation in dietary preparations used for the suppression of myocardial ^{18}F-FDG uptake in the diagnosis of CS. This systematic review suggests that carbohydrate restriction prior to cardiac PET scans may improve myocardial ^{18}F-FDG uptake suppression, however, while the studies concur in the identification of a broad dietary recommendation of a 'low carbohydrate' diet preparation, there is a distinct lack of specific dietary details available in the published literature.

For most studies identified in this review, the dietary preparation methodology was minimally described, making replication or cross-comparisons of these studies challenging. Varying cultural practices, food preferences and food availability internationally also makes replication of qualitative dietary preparation protocols difficult. There is limited or no reporting of adherence to the dietary recommendations or assessment of actual dietary intake and the dietary composition of 'unrestricted' or fasting only groups prior to their scans was not described and remains unknown.

Inconsistencies in study protocols are also apparent when analysing other aspects of PET preparation, including fasting times and length of time following a prescribed diet. While some studies have focused on preparatory guidelines specific to CS,[1,2,4,14] a number also reported using human study population groups with

Table 1. Summary of reviewed papers

Study Details and Quality of Evidence			*Analysis Method and Results*						*Notes*	
		Diet Details	*SUV*	*Statistical Significance*	*Clinical Significance*	*Visual Uptake Scale*	*Statistical Significance*	*Clinical Significance*	*Diet / Preparation*	*Analysis*
Sarcoidosis (human)										
Ambrosini et al. (2013)[14] *Evidence: Level III-3*			✓	NR	x	✓	NR	x		SUV_{max} of positive lesions Visual Uptake Scale: None; Diffuse; Focal; Focal on Diffuse
Group A (n=15)	Unrestricted diet + 6hr fast	NR								
Group B (n=28)	Fat Meal + 12hr fast	QT							2 examples of low carbohydrate foods provided. No other specific diet details provided.	
Lu et al. (2017)[4] *Evidence: Level III-3*			✓	NR	x	✓	S** p<0.001 (Group B vs Group A)	✓	All subjects had breakfast 4 hours prior to scan.	SUV_{max} of cardiac lesions Visual Uptake Scale: None; Ring Like Diffuse at Base (negative for CS); focal (positive for CS); and diffuse (indeterminate for CS) Group A: 5 out of 12 pts (41.7%) 'indeterminate' vs Group B: 7 out of 193 (3.6%) 'indeterminate'
Group A (n=12)	≤24hr High Fat High Protein Very Low Carb diet + 4hr fast	QL								
Group B (n=193)	**72hr High Fat High Protein Very Low Carb diet + 4hr fast**	QL								
Manabe et al. (2016)[2] *Evidence: Level III-1*			✓	NS (Group A vs Group B)	x	✓	S* p=0.0041 (Group B vs Group A)	✓	Both groups received IV heparin (50IU/kg).	SUV_{max} and Cardiac Metabolic Volume Visual Uptake Scale: Diffuse and Non-Diffuse
Group A (n=58)	≥6hr fast	NR								
Group B (n=24)	**Low Carb diet + ≥18hr fast**	QL and QT								
Scholtens et al. (2016)[1] *Evidence: Level III-3*						✓	S** p<0.0001 (Group B vs Group A)	✓	A third group (Group C, n=50) received IV (50 IU/kg) heparin in addition to Group B diet conditions (12hr Low Carb diet + 12hr fast). Results: significant improvement in cardiac suppression in the heparin group (Group C) "not only compared with the standard preparation (P<0.0001) but also compared with diet alone (P<0.0001). Adequate cardiac suppression (score ≤ 2) rose from 54% after diet alone to 88% after diet with heparin preadministration." (p.570)	Visual Uptake Scale: 0=uptake less than that in the liver) 1= Myocardium equal to left ventricular blood pool 2= Myocardium greater than left ventricular blood pool but less than liver 3= Myocardium focally greater than liver 4= Myocardium diffusely greater than liver <2 considered adequate suppression
Group A (n=50)	6hr fast	NR								
Group B (n=50)	**12hr Low Carb diet + 12hr fast**	NR								
Non-sarcoidosis (human)										
Balink et al. (2011)[11] *Evidence: Level III-3*						✓	S** P<0.0001 (Group B vs Group A)	✓		Visual Uptake Scale: 0=myocardial uptake less then liver uptake 1=myocardial uptake comparable with liver uptake 2=myocardial uptake considerably higher than liver uptake Different scanners used for each group: Group A – University Medical Center of Utrecht Group B – Medical Center Leeuwarden.
Group A (n=100)	1 day unrestricted diet + 6hr fast	NR								
Group B (n=100)	**1 day Fat and Protein Allowed Carb Restricted diet + 6hr fast**	QL and QT								
Cheng et al. (2010)[8] *Evidence: Level II*			✓	S* P=0.03 (Group B vs Group A) NS P=0.63 (Group C vs Group A)	✓					SUV_{max}
Group A (n=21)	≥6hr fast	NR							Group A: Allowed breakfast day of scan. Mean fasting time 745 mins/12 hours.	

Table 1. continued

Study Details and Quality of Evidence			*Analysis Method and Results*						*Notes*	
		Diet Details	*SUV*	*Statistical Significance*	*Clinical Significance*	*Visual Uptake Scale*	*Statistical Significance*	*Clinical Significance*	*Diet / Preparation*	*Analysis*
Group B (n=21)	**Low Carb dinner + overnight fast**	QT							Group B: Mean fasting time 899 mins/15 hours.	
Group C (n=21)	High Fat Low Carb dinner + overnightfast + Benecalorie ®	QT							Group C: Mean fasting time 61 mins/1 hour. Resource Benecalorie® beverage (no carb, 33g fat) 60-70 mins prior to scan.	
Coulden et al. (2012)[9] *Evidence: Level III-3*			✓	S* P<0.05 (Group B and C vs Group A) NS (Group B vs Group C)	✓				Diet intervention group (n= 120) divided into two groups for SUV analysis (Group B: Reported diet compliant and Group C: Reported diet non-compliant). No restriction on protein, fat, or calorie intake for any group.	SUV_{mean} and SUV_{max} Significant results ($P<0.05$) for myocardial SUV_{max}
Group A (n=120)	Overnight fast	NR								
Group B (n=26)	24hr Low Carb diet + overnight fast (non-compliant)	NR								
Group C (n=94)	**24hr Low Carb diet + overnight fast (compliant)**	QT								
Kobayashi et al. (2013)[10] *Evidence: Level IV* (n=14)			✓	S** P=0.001 (Protocol B vs Protocol A)	✓	✓	S* P=0.041 (Protocol B vs Protocol A)	✓	Same population group (n=14 'healthy volunteers') underwent scans after conventional (A) and modified (B) protocols. Half the dose of ^{18}F-FDG was administered in the modified diet (Protocol B).	SUV_{max} Visual Uptake Scale: 0= homogenously minimal 1=mostly minimal or mild uptake 2=mostly intense or moderate uptake 3=homogenously intense
Protocol A	≥6hr fast	NR							Protocol A: Mean fasting time 8.6hr (range 6.0-19.5hrs)	
Protocol B	**>24hr Carb Restricted diet + Atkins shake**	QT							Protocol B: Atkins Advantage Shake beverage (1g glucose, 9g fat) 1hr prior to injection.	
Shao et al. (2017)[5] *Evidence: Level III-2*			✓	S** P<0.001 (Group B vs Group A)	✓	✓	S** P<0.001 (Group B vs Group A)	✓	Group B: ^{18}F-FDG injection 4–5hrs after the meals. Protein permitted for meals.	SUV_{max} Visual Uptake Scale: 0= negligible myocardial uptake 1= minimal uptake with intensity similar to that of liver 2= moderate but inhomogeneous uptake 3= intense homogenous uptake
Group A (n=126)	≥12hr fast	NR								
Group B (n=126)	**24hr Carb Restriction + 2x Low Carb High Fat meals**	QL								
Williams and Kolodny (2008)[6] *Evidence: Level III-3*			✓	S** P<0.000001 (Group B vs Group A)	✓	✓	NR	✓	Group B: Time from consumption of meal to ^{18}F-FDG injection ranged from <2 hours to 12 hours.	SUV_{min} and SUV_{max} Significant result from myocardial SUV_{max} analysis.
Group A (n=101)	≥4hr fast	NR								Visual Uptake Scale: 0= homogeneously minimal 1= mostly minimal or mild uptake 2= mostly intense or moderate uptake 3= homogeneously intense.
Group B (n=60)	**Very High Fat Low Carb Protein Permitted meal**	QL							Subjects in Group B who reported diet non-adherence (n= not reported) were excluded from analysis.	
Wykrzykowska et al. (2009)[7] *Evidence: Level III-3*			✓	S** P<0.001 (Group B vs Group A)	✓				A third group (Group C, n=32) were also scanned following Group B diet conditions. Results: 63% of patients had good or adequate myocardial suppression and interpretable scans. Statistical significance not reported.	SUV_{max} Group C only – Visual Uptake Scale: 0=poor 1=adequate 2=good
Group A (n=1229)	≥8hr fast	NR								
Group B (n=724)	**Low Carb High Fat meal + ClearScan**	QL							ClearScan (E-Z-EM Inc) described as 'vegetable oil drink' – nutritional information not available.	

Table 1. continued

Study Details and Quality of Evidence			*Analysis Method and Results*						*Notes*	
		Diet Details	*SUV*	*Statistical Significance*	*Clinical Significance*	*Visual Uptake Scale*	*Statistical Significance*	*Clinical Significance*	*Diet / Preparation*	*Analysis*
Non-sarcoidosis (animal)										
Cusso et al. (2014)[12] *Evidence: Level IV* (n=10 mice)			✓	S* P=0.008 (Protocol C vs Protocol A) S* P=0.015 (Protocol B vs Protocol A) NS (P=0.626 Protocol C vs Protocol B)	✓	✓	S* P=0.037 (Group C versus Group B)	✓	Qualitative diet details unable to be provided for animal study. All mice (n=10) underwent four scans after: regular diet (Protocol A); sunflower seed diet (Protocol B); ketogenic diet (Protocol C); and administration of a single intraperitoneal dose of verapamil (1.3mg/kg) (Protocol D). Mice returned to their regular diet (Protocol A) for four days between each treatment or change in diet. Protocol D not listed in table as no diet intervention. Results: SUVmean: NS (Protocol D vs Protocol A) Visual Uptake Scale: S* P=0.013 (Protocol D vs Protocol B)	Myocardial SUV_{mean} Visual: 0= homogeneously minimal 1= mostly minimal or mild 2= mostly intense or moderate 3= homogeneously intense
Protocol A	4 days Regular diet	QT							Protocol A (AO4, SAFE diet): 72.4% carb / 8.4% fat / 19.3% protein	
Protocol B	2 days Sunflower Seed diet	QT							Protocol B (Euricar Europa, S.L. diet): 18% carb / 55% fat	
Protocol C	**2 days Ketogenic diet**	QT							Protocol C: (TD 96355,Harlan diet): 0.4% carb / 90% fat	
Fine et al. (2009)[13] *Evidence: Level II* (n=15 rats)			✓	S** p<0.001 (Protocol C vs Protocol B and Protocol A) NS (P=0.99 Protocol B vs Protocol A)	✓				Qualitative diet details unable to be provided for animal study. All rats (n=15) had 2 weeks of a 'standard rodent diet' (Lab Diet Inc. Diet 5001): 58% carb / 13.5% fat / 28.5% protein) before randomised switching into one of the three diet groups (Protocol A, B or C). All rats underwent three scans after: high carb diet (Protocol A); intermediate carb diet (Protocol B); and low carb diet (Protocol C).	Mean myocardial $SUV_{max.}$
Protocol A (n=5)	4 weeks High Carb diet	QT							Protocol A (Research Diets Diet D12359): 78% carb / 2% fat 20% protein	
Protocol B (n=5)	4 weeks Intermediate Carb diet	QT							Protocol B (Harlan Teklad Diet 8664): 52% carb / 28% fat / 20% protein	
Protocol C (n=5)	**4 weeks Low Carb diet**	QT							Protocol C (Research Diets Diet D12369B): 0.01% carb / 90% fat / 10% protein	
(n=4 mice)				S* P<0.03 Protocol A vs Protocol B					Four mice were also studied – all given 2 weeks of standard diet (Protocol A) followed by 4 weeks of low carb diet (Protocol B).	Mean SUV_{max} Significant result from myocardial SUV_{max} analysis.
Protocol A	2 weeks Standard diet								Protocol A (Lab Diet Inc. Diet 5001): 58% carb / 13.5% fat / 28.5% protein)	
Protocol B	**4 weeks Low Carb diet**								Protocol B (Research Diets Diet D12369B): 0.01% carb / 90% fat / 10% protein	

Bolded group represents the most improved group
NR, not reported; *QT*, quantitative; *QL*, qualitative; *NS*, not significant
✔ = Reported/analysed
S* = $P \leq 0.05$
S** = $P \leq 0.001$

oncological non-cardiac pathologies[6,8,9,11] or healthy volunteers [10] as well animals.[12,13]

The two animal studies provided more specific dietary detail than the human studies, including a description of the macronutrient contribution of fat and protein (not just carbohydrate) in the preparation diets, however the degree of carbohydrate restriction required to achieve optimal interpretation is not known. In the Fine et al. study[13] it appears carbohydrate should provide between 0.01% and 52% of total energy intake and the Cusso et al. study[12] suggests carbohydrate should be restricted to between 0.4% and 18% of total energy—the ideal amount of carbohydrate restriction within these ranges is not clear. Despite these studies providing greater dietary detail, it would be difficult to replicate the specificity of these animal diets in humans, especially considering the length of time the preparation diets were used (2 days to 4 weeks).[12,13] Human scan subjects are also unlikely to be compliant with such strict dietary preparation protocols, especially when considering meal preparation skills and dietary palatability.

Variations in the measures of scan acceptability were evident. In some studies, statistical and clinical significance was attained via quantitative or objective measurements (SUV) as well as via qualitative or subjective measurements (visual uptake scale). In addition to different SUV (SUV_{mean}, SUV_{max} or SUV_{min}) measurements being reported, SUV regions across the various studies were drawn in different prescribed anatomical locations within the heart and were of varying sizes and shape depending on the study analysis method. All of these variances would have a significant impact on the SUV results generated. Different visual uptake scales (two-point,[2] three-point,[11] four-point [4–6,10,12,14], and five-point scales [1]) were used by studies to assess the cardiac uptake present in the images. The implications of these variances could be significant, particularly in clinical practice where scan interpretation relies heavily on adequate suppression of physiological cardiac uptake. Other complicating factors include an inability to accurately replicate and compare images or results acquired at different imaging facilities. This in turn creates issues in assessing disease progression and accurately determining the success of treatment regimes. The variation in tools and the inherent issues that arise with subjective measures, makes direct comparisons of study outcomes difficult.

The dietary preparations found to be effective for sufficient ^{18}F-FDG uptake suppression to enhance PET interpretation varied greatly both quantitatively and qualitatively, meaning the optimal carbohydrate restriction or dietary macronutrient composition remains unclear. Also unknown is the optimal period of time for maintaining a specific dietary prescription prior to a scan. The large variances between dietary preparations used in these reviewed studies underscore the lack of consensus or gold standard for patient preparation in this application of ^{18}F-FDG PET imaging.

In October 2017 the Society of Nuclear Medicine and Molecular Imaging (SNMMI) and the American Society of Nuclear Cardiology (ASNC) published the 'Joint SNMMI–ASNC expert consensus document on the role of ^{18}F-FDG PET/CT in cardiac sarcoid detection and therapy monitoring'.[15] This joint statement identified ''on the basis of the current literature and our expert consensus, the most common components in preparing patients to undergo ^{18}F-FDG PET for inflammation include prolonged fasting, dietary manipulation, and intravenous heparin, often in combination.'' These authors also acknowledge that ''the optimum amount of fat or carbohydrate in these dietary manipulations has not been clearly defined or standardized.'' In this joint statement, the SNMMI and ASNC outline two options for patient preparation for an ^{18}F-FDG PET scan for cardiac sarcoidosis. The ''preferred option'' is the consumption of at least two high fat (> 35 g), low carbohydrate (< 3 g) meals the day before the study with a fast of at least 4-12 hours. The alternative option is a fast of more than 18 hours.

This joint statement references the Cheng et al. article[8] in its prescription of meals with > 35 g of fat and < 3 g of carbohydrate, however, as outlined in Table 1, the only significant result found in this study was when comparing the low carbohydrate only group (meal with < 5 g carbohydrates) with the fasting only group (unrestricted diet, fast for 6 hours prior to scan). Comparison between the fasting only group and the high fat, low carbohydrate group (meal with < 5 g carbohydrate and > 35 g fat plus Benecalorie drink) found no significant differences in uptake suppression. The expert consensus guidelines[15] state that ''one study did specify that the evening meal before the PET study should include more than 35 g of fat and less than 5 g of carbohydrates'' (referring to the Cheng et al. paper[8])—a statement on the dietary preparation used for this particular study—however this dietary preparation did not significantly improve scan results. Therefore, it does not appear there is any convincing evidence that this particular dietary preparation should be routinely utilized.

Other studies found in this literature review which investigated the role of fat within the dietary preparation for ^{18}F-FDG PET were:

- Lu et al.[4] which lists some high fat foods (e.g., butter, cheese, oil) within the ''encouraged/permitted foods'' however does not specify an amount of fat to be consumed. As such, a subject could still avoid all prohibited foods, without consuming high amounts of fat.

- Shao et al.[5] which qualitatively describes a low carbohydrate and high fat meal, however the diet instructions provided do not mention the addition of any fat or even what would be considered high fat foods. The only suggested ''edible'' foods are ''fish/meat (beef or pork); fried eggs; scrambled eggs.''
- Kobayashi et al.[10] which suggests a meal with ''< 10 g glucose and > 35 g fat'' plus an Atkins shake (1 g glucose and 9 g fat) 1 hour before the scan. This preparation protocol is compared with a 6 hour fast only. It is not explored whether the high fat meal or the Atkins shake might improve uptake suppression independently of one another or within some other diet/supplement combination.
- Williams and Kolodny[6] use similar instructions as Lu et al. in that a 'high fat' diet is described, however within the ''permitted foods'' (low carbohydrate foods), only a small number would be considered high fat (e.g., bacon, sausages). In addition, some ''non-permitted'' foods are actually low in carbohydrates and high in fat (e.g., cheese, nuts). Again, patients in this study could have therefore avoided consuming a 'high fat' diet while still complying with the dietary preparation specified.
- Wykrzykowska et al.[7] use the same dietary guidelines as Williams and Kolodny [6] but also add a ''ClearScan'' supplement drink—this is described as a ''vegetable oil drink'' however no nutritional information is available for this supplement.

The SNMMI and ASNC joint statement[15] recommends a fast of more than 18 h in preparation for ^{18}F-FDG PET if dietary manipulation is not possible. We have previously commented on the vast range of fasting times used both within and between the studies reviewed and note that fasting time likely has a significant role in ^{18}F-FDG uptake suppression. As our selection criteria specified the exclusion of studies which compared fasting times alone, it is not within the scope of this paper to further deliberate these findings.

The current practices of cardiac PET scan preparation diets are variable and due to the quality of the study designs used by the reviewed papers and the lack of comparability between study results, the overall level of evidence for the dietary preparation prior to cardiac PET scans is weak. It should be noted that while some level of dietary carbohydrate restriction appears to be routinely recommended in practice prior to cardiac PET scans for investigation of CS, this review identified only four published studies which analyzed ^{18}F-FDG uptake suppression for diagnosing CS. This indicates that the evidence in the published literature for dietary preparation prior to CS diagnostic scans is especially poor.

NEW KNOWLEDGE GAINED

Overall, the low study quality and frequent absence of dietary macronutrient composition or dietary adherence details limits the conclusions that can be drawn regarding dietary changes to optimize ^{18}F-FDG PET readability. The studies analyzed in this systematic review suggest improvements in PET scan readability following:

(i) fasting and a low carbohydrate intake (definition of a low carbohydrate intake varying greatly in each study) with no conclusive evidence of additional benefit if fats added;
(ii) restricting carbohydrate containing foods for a longer time period (72 vs 24 hours[4]); and
(iii) ketogenic and very low carbohydrate diets (0.01% to 0.4% of total kilojoule intake[12,13]) within animal models.

CONCLUSIONS

A definitive dietary preparation recommendation is not possible based on current evidence, however, scan readability does seem to be improved when preparation includes a reduced carbohydrate intake. More robustly designed studies involving specified cardiac pathologies and ensuring replicable dietary preparations are now needed to identify the ideal dietary macronutrient composition, length of dietary preparation and length of pre-scan fasting required for optimal suppression of myocardial ^{18}F-FDG uptake for cardiac PET scans.

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Disclosure

The authors have declared no conflicts of interest.

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