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Editorial

GLP-1 Receptor Agonists: An Emerging Pitfall in FDG PET/CT Interpretation

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Abstract

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are increasingly used for type 2 diabetes and obesity, but recent reports indicate they can alter FDG biodistribution on PET/CT, creating potential pitfalls in oncologic imaging. Atypical uptake may occur in skeletal muscle, brown adipose tissue, and the gastrointestinal tract, mimicking inflammatory or malignant processes. These pharmacologically induced patterns can lead to diagnostic uncertainty, unnecessary investigations, and inappropriate management decisions. Recognizing the mechanisms — delayed gastric emptying, brown fat activation, and altered insulin-sensitive tissue uptake — is critical for accurate image interpretation. Integrating medicine-related information in daily PET/CT planning and being aware of GLP-1 RA use throughout the process of image processing could potentially help decrease diagnosis-related uncertainty. Imaging professionals and nuclear treatment experts need to be mindful of these possible implications in an effort to decode oncological images in individuals receiving GLP-1 therapy with care.

More Information

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Dear editor,

The clinical use of glucagon-like peptide-1 receptor agonists (GLP-1 RAs) has expanded substantially in recent years for the management of type 2 diabetes and obesity [1]. Emerging reports have described potential alterations in 18F-fluorodeoxyglucose (FDG) biodistribution in patients receiving GLP-1-based therapies, including increased skeletal muscle and myocardial uptake and increased brown adipose tissue (BAT) activity, which may occasionally complicate PET/CT interpretation [2,3,5]. However, the available evidence remains limited and is largely based on case reports, small series, and early observational data. With the increasing use of these medications among patients undergoing oncological imaging, awareness of possible medication-related alterations in tracer distribution may be relevant to PET/CT interpretation, although their frequency and clinical significance remain incompletely characterized.

Reports describing altered FDG uptake in patients receiving GLP-1 RAs remain limited. Published observations have included increased uptake in skeletal muscle, myocardium, brown adipose tissue, and gastrointestinal structures. These findings may complicate interpretation when the distribution resembles inflammatory or malignant disease.

Importantly, the evidence should be distinguished from the established pharmacological effects of GLP-1 RAs. Delayed gastric emptying is a well-established consequence of GLP-1 receptor activation and may contribute to retained luminal activity within the stomach and bowel. In contrast, the extent to which GLP-1 RAs directly produce clinically meaningful alterations in FDG biodistribution remains uncertain. Current observations therefore represent preliminary imaging findings rather than definitive evidence of a reproducible class effect.

Several factors may contribute to these findings. Delayed gastric emptying is a well-established effect of GLP-1 receptor agonists and has been documented in clinical studies and

recent meta-analyses [4,7]. These effects may contribute to retained luminal FDG activity in the stomach and bowel; however, the extent to which GLP-1 receptor agonists produce tumor-mimicking FDG uptake on PET/CT remains preliminary and is supported primarily by limited clinical reports. In a single-patient case report involving semaglutide, increased FDG uptake in brown adipose tissue in the cervical and supraclavicular regions mimicked metastatic head and neck cancer on PET/CT [3]. Thus, the potential for GLP-1 receptor agonist–associated BAT activation to create a false-positive oncologic appearance should be regarded as a preliminary imaging observation rather than an established class effect. In addition, effects on insulin secretion and glucose metabolism may alter FDG biodistribution in insulin-sensitive tissues, although the clinical significance of these effects in patients receiving GLP-1 receptor agonists remains incompletely characterized [2,5].

These effects may introduce interpretative challenges. Unlike metformin-associated gastrointestinal FDG uptake, which is well established in the literature, evidence for altered FDG biodistribution with GLP-1 receptor agonists remains limited and preliminary [6]. In a case report involving semaglutide, increased FDG uptake in skeletal muscles and the myocardium complicated PET interpretation and was considered potentially medication-related [5]. Similarly, the single-patient case report by Harrison et al. involving semaglutide described increased FDG uptake in brown adipose tissue that mimicked metastatic disease [3]. These observations suggest that GLP-1 receptor agonists may affect FDG biodistribution in selected patients; however, current evidence is insufficient to establish these findings as consistent effects across the GLP-1 receptor agonist class. Importantly, emerging data suggest that the clinical impact of these effects may be variable. A recent study comparing patients on GLP-1 receptor agonists with matched controls (n = 30 per group) did not demonstrate a significant effect of semaglutide on FDG PET image quality, highlighting the need for cautious interpretation of existing reports and further large-scale evaluation [8].

Clinical implications and PET/CT preparation

Current PET/CT preparation guidance does not establish a specific withholding interval for GLP-1 receptor agonists before FDG PET/CT. Although treatment discontinuation has been described in individual circumstances, available evidence is insufficient to determine whether withholding therapy improves PET/CT image quality or to define an optimal interval.

Routine discontinuation of GLP-1 RAs solely for FDG PET/CT preparation should therefore not be recommended on the basis of the currently available evidence. If temporary interruption is considered for an individual patient, the decision should take into account the specific agent, dosing interval, pharmacokinetic characteristics, indication for treatment, and potential consequences of treatment interruption. In patients with diabetes, interruption may affect glycemic control, while interruption in patients receiving treatment for obesity may disrupt an established therapeutic strategy.

Documentation of GLP-1 RA use and communication between the treating team and nuclear medicine professionals may currently represent a more evidence-consistent approach than routine treatment discontinuation.

Current PET/CT preparation guidelines do not establish a specific withholding interval for GLP-1 receptor agonists before FDG PET/CT [9]. Although temporary discontinuation has been described in individual cases, current evidence is insufficient to determine whether withholding GLP-1 RAs improves PET/CT image quality or to define an optimal interval before imaging. Therefore, routine discontinuation solely for FDG PET/CT preparation cannot currently be recommended. If temporary discontinuation is considered, the decision should be individualized according to the specific GLP-1 RA, its pharmacokinetic properties, dosing interval, and duration of action, in consultation with the treating clinician. Interruption of therapy may also have clinical consequences, including loss of glycemic control in patients with type 2 diabetes and disruption of ongoing obesity-management strategies. Antidiabetic medications may also influence FDG biodistribution; for example, metformin is associated with increased intestinal FDG uptake [10]. These potential risks should be weighed against any uncertain imaging benefit before treatment is withheld.

In conclusion, GLP-1 receptor agonists may represent a potential, but incompletely characterised, factor influencing FDG biodistribution. Current evidence remains limited and does not establish the prevalence, reproducibility, or clinical significance of these observations. Further prospective studies are required to clarify whether GLP-1 receptor agonists have clinically meaningful effects on FDG PET/CT interpretation and whether any modifications to imaging preparation or protocols may ultimately be warranted.

Conclusion

GLP-1 receptor agonists may represent a potential medication-related factor influencing FDG biodistribution in selected patients, but the current evidence remains limited and incompletely characterized. Reported abnormalities involving skeletal muscle, myocardium, brown adipose tissue, and gastrointestinal structures are supported primarily by case reports and small studies and should therefore be interpreted cautiously.

At present, there is insufficient evidence to recommend routine discontinuation of GLP-1 receptor agonists before FDG PET/CT or to define an optimal withholding interval. Documentation of GLP-1 RA use and awareness of possible

medication-related uptake patterns may provide a more appropriate approach while further evidence is generated. Prospective, adequately powered comparative studies are needed to determine the prevalence, reproducibility, clinical significance, and potential management implications of these observations...

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