

## Systematic Review

Anxiety experienced by oncological patients who undergo  $^{18}\text{F}$ -FDG PET CT: A systematic reviewL. Vieira <sup>a, b, \*</sup>, A. Pires <sup>c, d</sup>, A. Grilo <sup>a, e</sup><sup>a</sup> H&TRC-Health & Technology Research Center, ESTeSL-Escola Superior de Tecnologia da Saúde, Instituto Politécnico de Lisboa, Lisbon, Portugal, Av. D. João II, Lote 4.69.01, Parque das Nações, 1990-096, Lisboa, Portugal<sup>b</sup> CIMOSM – Centro de Investigação em Modelação e Optimização de Sistemas Multifuncionais, Instituto Superior de Engenharia de Lisboa, Instituto Politécnico de Lisboa, Rua Conselheiro Emídio Navarro, 1, 1959-007 Lisboa, Portugal<sup>c</sup> Escola Superior de Tecnologia da Saúde, Instituto Politécnico de Lisboa, Av. D. João II, Lote 4.69.01, Parque das Nações, 1990-096, Lisboa, Portugal<sup>d</sup> Faculdade de Medicina Dentária, Universidade de Lisboa, Rua Professora Teresa Ambrósio, Cidade Universitária, 1600-277, Lisbon, Portugal<sup>e</sup> Centro de Investigação em Ciência Psicológica, Faculdade de Psicologia, Universidade de Lisboa, Alameda da Universidade, 1649-013, Lisboa, Portugal

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## ABSTRACT

**Introduction:** Anxiety is an emotional reaction often experienced by patients who undergo Positron Emission Tomography/Computed Tomography (PET/CT) with  $^{18}\text{F}$ -2-fluoro-2-deoxy-D-glucose ( $^{18}\text{F}$ -FDG). This systematic review aimed to summarise the evidence currently available considering the anxiety experienced by adult oncological patients concerning pre and post  $^{18}\text{F}$ -FDG PET/CT examination and the factors contributing to anxiety.

**Methods:** A systematic review search of CINAHL, PsycINFO, PubMed, Scopus and Web Science databases and other manual search sources, was conducted from November to February 2021. The research included articles published from January 2000 to December 2020. It included quantitative studies, which analysed the anxiety experienced by oncological patients who had undergone  $^{18}\text{F}$ -FDG PET/CT.

**Results:** Ten articles met the inclusion criteria for this systematic review. The studies selected were published between 2011 and 2020 and carried out in five countries. Anxiety experienced by patients was evaluated at the various stages of the  $^{18}\text{F}$ -FDG PET/CT, eight studies assessed it in the pre-examination, seven studies in the post-examination and five studies at both times. Four main anxiety factors were found: patients' clinical situation, first-time patients' examination, scan procedure, and patients concern with the examination result.

**Conclusion:** Moderate to high levels of anxiety are present in most of the patients who undergo the examination. This review also highlights several factors related to the anxiety levels through different procedure moments.

**Implications for practice:** The results of this research will allow health professionals to adjust non-pharmacological strategies to decrease anxiety levels in oncological patients undergoing  $^{18}\text{F}$ -FDG PET/CT.

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## Introduction

Imaging of Nuclear Medicine (NM) can contribute to the diagnosis, staging and/or evaluation of the response to therapy in oncology. Among the various examinations, Positron Emission Tomography/Computed Tomography (PET/CT) stands out as simple to

perform and minimally invasive and painless. This imaging technique is relevant in oncology, for the contributions described above, and to help in the delimitation of tumour volumes in Radiotherapy planning.<sup>1,2</sup>

PET/CT is an imaging technique that may use several radiopharmaceuticals depending on the intended study.<sup>2,3</sup>  $^{18}\text{F}$ -2-fluoro-2-deoxy-D-glucose ( $^{18}\text{F}$ -FDG) is the most widely used radiopharmaceutical in PET/CT, in the NM departments.<sup>4,5</sup>

The FDG molecule is characterised by being a glucose analogue, coupled with radioisotope  $^{18}\text{F}$ . For this reason, it is biodistributed to the organs that consume the most glucose, namely: brain, heart, kidneys, ureters, and bladder. The uptake of  $^{18}\text{F}$ -FDG in the cerebral

\* Corresponding author. H&TRC-Health & Technology Research Center, ESTeSL-Escola Superior de Tecnologia da Saúde, Instituto Politécnico de Lisboa, Lisbon, Portugal, Av. D. João II, lote 4.69.01, Parque das Nações, 1990-096, Lisboa, Portugal.

E-mail addresses: [lina.vieira@estesl.ipl.pt](mailto:lina.vieira@estesl.ipl.pt) (L. Vieira), [anafilipa.abt@gmail.com](mailto:anafilipa.abt@gmail.com) (A. Pires), [ana.grilo@estesl.ipl.pt](mailto:ana.grilo@estesl.ipl.pt) (A. Grilo).

cortex, gastrointestinal system, muscles and in the areas of the liver, spleen and bone marrow can also be considered normal if patients have been submitted to other stimulant factors. However, as most cancer cells have high glycolytic activity, it can easily be inferred that the uptake of  $^{18}\text{F}$ -FDG will be higher in these cells and, consequently, the image appears with higher uptake of the radiopharmaceutical in the tumour cells when compared to normal cells, thus making it possible to distinguish between normal tissue and pathological tissue.<sup>1–5</sup>

A patient who undergo an  $^{18}\text{F}$ -FDG examination with PET/CT will have to go through several steps. The first step is related to the previous preparation that the patient will have to do for the examination. The next step is the arrival of the patient at the NM Department, and the last step is the acquisition of the images.

Considering the first step, the patient must not take any sports activities during the 6 h before the examination and must present himself on the day of the examination with a 4–6 h fast.<sup>1</sup> Second, and after admitting the patient at the NM Department and before the radiopharmaceutical injection, the glycemic value is measured. Once the radiopharmaceutical is administered intravenously, the patient waits 30–60 min in a post-injection room.<sup>1</sup> Finally, the patient will undergo the examination in the PET/CT tomograph. The images acquisition varies between 15–60 min, depending on the requirement of additional images.<sup>1,5,6</sup>

Anxiety is a complex emotion, felt in a potentially dangerous or unknown situation for the individual.<sup>7</sup> It can take many forms, as physiological, psychological, or behavioural components.<sup>8,9</sup> Anxiety is commonly visible in physiological symptoms such as muscle tension, fatigue, tremors, frequent urination, and variations in blood glucose levels. Psychologically, there is the possibility of a decrease in the perception of self-efficacy, discomfort, or irritability. On a behavioural level, it is associated with a constant movement by the patient.<sup>10–12</sup>

Several factors enhance anxiety in patients who undergo PET/CT. Acuff et al. (2014)<sup>13</sup> and Grilo et al. (2017)<sup>14</sup> pointed out as factors contributing for a high level of anxiety: the concern with the diagnosis and the possible change in the treatment strategy. Besides, anxiety is further intensified by lack of knowledge about the procedure, use of radiopharmaceuticals (due to radiation), claustrophobia, patient difficulty in speaking or listening during the examination, and the whole duration of the procedure.<sup>6,15</sup>

Anxiety contributes to a patient's negative experience of the PET/CT examination, and increases the likelihood of false positives, compromising the quality of images.<sup>16,17</sup> During the examination, the patient's anxiety makes it more difficult for him to remain motionless, leading to artefacts in the images and consequently to misdiagnoses. Artefacts may also arise because the patient is not relaxed (muscle tension) and, therefore, has a higher radiopharmaceutical uptake in the muscles and brown fat.<sup>1,14</sup> Also, anxiety found in some patients increase health care professional pressure related to tranquillise the patient and the concern with artefacts' possible presence.<sup>18</sup>

To our knowledge, no systematic review has been previously conducted focusing on the anxiety experienced by oncological patients who undergo PET/CT. The synthesis of the scientific evidence is of major clinical importance since it will assist health professionals in NM Departments to better understand the anxiety experienced by oncological patients undergoing PET/CT, and the factors contributing to anxiety. Accordingly, health professionals may reflect on the most appropriate methods to support patients considering their anxiety pre and post PET/CT examination. The review will also contribute to pointing out new approaches for future investigations. Therefore, this systematic review aims to summarise currently available evidence considering anxiety experienced by adult oncological patients concerning pre and post  $^{18}\text{F}$ -FDG PET/CT examination and the factors contributing to anxiety.

## Methods

### Design

A systematic literature review of quantitative studies was performed to understand adult oncological patient anxiety experienced in pre and post  $^{18}\text{F}$ -FDG PET/CT examinations and the factors contributing to anxiety. The review was conducted taking into consideration the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA), which encompass four phases: Identification, Screening, Eligibility, and Inclusion (Fig. 1).<sup>19</sup>

### Search strategy

Publications which describe original quantitative research were retrieved via electronic database searches of CINAHL, PsycINFO, PubMed, Scopus, Web of Science, and other manual search sources, in the period from November to February 2021. The research included articles published from January 2000 to December 2020. The keywords used with the Boolean operator AND were: “patient anxiety”; AND “PET CT” AND “oncology” for all the above research bases. We considered for analysis all articles, published in Portuguese, English and Spanish that assess anxiety experienced pre and/or post  $^{18}\text{F}$ -FDG PET/CT of at least one group of oncological patients who underwent PET/CT with  $^{18}\text{F}$ -FDG scan, without any anxiety intervention. No minimum number of patients was considered for the selected studies. With access to their full text, all articles found were included as shown in Fig. 1.

### Eligibility criteria

Original quantitative research papers were evaluated for inclusion or exclusion based on PICO<sup>20</sup> criteria detailed in Table 1.

### Quality appraisal

The systematic review method developed by Hawker et al. (2002)<sup>21</sup> was used to assess the quality of the included studies in nine dimensions. Two authors (LV and AP) evaluated all articles independently in each dimension, as “good”, “fair”, “poor” and “very poor”. Each study could have a score ranging from 9 to 36 points. Disagreement assessments between the three authors were discussed until a consensus found (Table 2).

### Data extraction

The data were extracted from all articles independently by two reviewers. For each study, information was extracted regarding the authors, year of publication, country, sample, study design, measures/instruments, and anxiety results (Table 2).

## Results

### Study selection

A total of 100 studies were identified in five databases. After removing the duplicate studies, books chapters, reviews, proceedings, and letters, 53 reports were reviewed for inclusion and nine met the inclusion criteria. Subsequently, a further report was found by manual search and included. In total, ten articles were included in this review, as illustrated in Fig. 1.

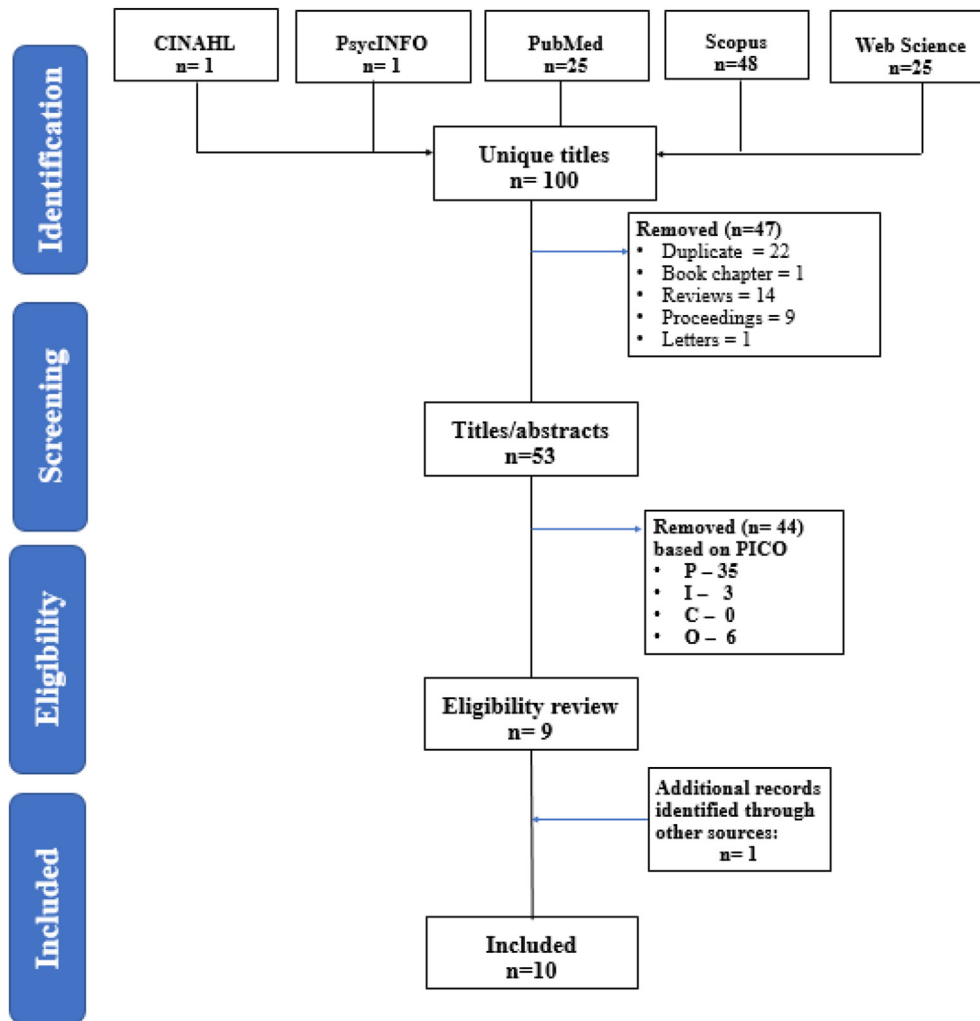


Figure 1. Search and study selection PRISMA flow diagram.

Table 1

PICO criteria for inclusion and exclusion in systematic review.

Parameters	Inclusion Criteria	Exclusion Criteria
P – Population	Adult oncological patients	Pediatric patients
I – Intervention	PET/CT with <sup>18</sup> F-FDG	PET/CT with other radiopharmaceuticals
C – Comparison	Not applicable	Not applicable
O – Outcomes	Anxiety measures Factors contributing to anxiety	– Articles that do not include any form of anxiety assessment

### Characteristics of included studies

Ten articles have been studied to analyse anxiety experienced and the factor(s) contributing to anxiety. Their characteristics are illustrated in Table 2.

The studies selected were published between 2011 and 2020, and carried out in five countries, China,<sup>27</sup> Netherlands,<sup>18,24</sup> Portugal,<sup>14,15,23,26</sup> Spain,<sup>7,23,25</sup> and Turkey.<sup>22</sup> Considering methodological quality assessment, no study was excluded; eight studies were rated as good<sup>7,14,15,18,22,24,26,27</sup> and two as fair.<sup>23,25</sup>

All studies included oncological patients in samples studied. But specifically, Goense et al. (2018)<sup>24</sup> restricted their study to oncological patients with newly diagnosed oesophageal cancer. These samples ranged from a minimum of 22 individuals<sup>23</sup> to a maximum of 232.<sup>15</sup>

The studies included were all quantitative, presenting different instruments to measure anxiety. Eight of the studies used the Spielberger State-Trait Anxiety Inventory (STAI),<sup>7,14,22,23,25–27</sup> which is a standardised questionnaire. In these studies, different versions of STAI were used, namely (i) STAI-S,<sup>7,14,22,25–27</sup> (ii) STAI-T<sup>7,22,25,27</sup> and (iii) STAI-S brief.<sup>18,23</sup> Regarding STAI-S brief, it shall be noted that a scale from 8 to 32 points was used in study Vogel et al. (2012),<sup>18</sup> and a scale from 0 to 24 points was used by Santos et al. (2018).<sup>23</sup> Additionally, one other questionnaire was added in six of the mentioned eight studies: an Scan Experience Questionnaire (SEQ) was used in three studies,<sup>14,23,26</sup> an ad hoc questionnaire (adHQ) was used in study Lorca et al. (2019),<sup>25</sup> a Hospital Anxiety Depression Scale (HADS) questionnaire was used by Elboga et al. (2015)<sup>22</sup> and a Patient Experience Questionnaire (PEQ), which is a standardised questionnaire developed by Pettersen et al. (2004)<sup>28</sup>

**Table 2**

Characteristics and Quality Appraisal of the ten scientific articles included in the review.

Author, Year and Country	Sample	Design of study	Measures/Instruments	Anxiety Results			Quality appraisal <sup>15</sup>
				Pre-examination	Post-examination	factor(s) contributing to anxiety	
Pifarré et al. (2011), Spain <sup>7</sup>	200 Oncological Patients	Pre-examination - 2 groups: a. patients who made for the first time <sup>18</sup> F-FDG PET/CT (66.5%) b. patients who had already undergone <sup>18</sup> F- FDG PET/CT (33.5%).	STAI – S (scale of 0–60) STAI – T (scale of 0–60)	67.5% (n = 135) patients experience anxiety; o 70.0% (n = 93) of that 133 patients who underwent the examination for the first time were anxious. o 62.7% (n = 42) of that 67 patients who had previously performed the examination were anxious.		Clinical situation - % of anxious patients: o Initial staging (79.0%); o Tumor recurrence (72.7%); o Characterization (38.0%); o Disease control (36.6%); Gender: o Men (84.6%).	31
Vogel et al. (2012), Netherlands <sup>18</sup>	50 Oncological Patients	Pre-examination (at the beginning of the uptake period); Post-examination (at the end of the uptake period)	STAI-S – brief - (scale of 8–32) Physiologic parameters: o Cortisol concentration. o Heart Rate. o Muscle Activity. o Skin conductance level o uptake in muscles o uptake in Brown adipose tissue	59.9% highly anxious at uptake room. o Patients who underwent the examination for the first time were more anxious than patients who had already performed the examination previously.	o Reduction of anxiety values measured by STAI. o Reduction of physiological measures: Salivary cortisol concentration (µg/dl) and Heart Rate. o Increase in Skin conductance value.	First time – patients undergoing <sup>18</sup> F-FDG PET/CT. Scan procedure: o Discomfort due to the temperature of uptake room - where patients rest after the injection of the radiopharmaceutical.	32
Elboga et al. (2015), Turkey <sup>22</sup>	144 Oncological Patients	Pre-examination (before the injection)	STAI-S (scale 20-80) STAI-T (scale 20-80) HADS	STAI-S - Mean ± SD - 40.4 ± 8.5 STAI-T - Mean ± SD - 46.6 ± 7.8 HADS – Mean ± SD - 9.2 ± 3.8		Clinical situation: Patients at a higher stage of the disease were more anxious than earlier stage (STAI -45.2 ± 9.8/ 42.6 ± 10.06) Gender: o Women (STAI-S 45.4 ± 7.0; HADS 9.1 ± 3.6) There was a statistically significant difference between women and men. Smoking: o Não smokers have higher anxiety than smokers (STAI -38.124 ± 9.6/41.4 ± 10.02 HAD -7.761 ± 3.3/8.4 ± 2.9) Gender (in post examination): o Men have higher levels of anxiety. Scan procedure: o Effects of radiation.	32
Abreu et al. (2016), Portugal <sup>15</sup>	232 Oncological Patients	Pre-examination (on arrived at Department and prior to any information from the Health Professional) Post-examination (after the end of image acquisition)	SEQ Anxiety Subjective Thermometer, (10-point Likert scale).	Mean ± SD - 6.4 ± 2.7 Statistically Significant difference between pre and post examination anxiety values. Gender: o Men vs Women - no significant difference in the subjective perception of anxiety before the procedure (U = 5803.5, p = 0.07).	Mean ± SD - 5.7 ± 2.6.  Gender: o Men vs Women - significant difference in the subjective perception of anxiety after the procedure (U = 5641, p = 0.033), with men presenting higher values.		34

5	Grilo et al. (2017), Portugal <sup>14</sup>	81 Oncological Patients	Pre and post-examination	STAI-S (scale 0–60); SEQ	STAI-S – Mean $\pm$ SD - 31.1 $\pm$ 5.2 82.7% of patients were anxious: o 79.1% results; o 11.9% scan procedure; o 3% illness.	STAI-S- Mean $\pm$ SD – 33.9 $\pm$ 4.2 75.3% of patients were anxious: o 86.9% results; o 6.6% scan procedure; o 1.6% illness.	Concern with the result of the examination. Scan procedure: o Discomfort during image acquisition (rigid body position, with the arms positioned in a restricted space - significant low positive correlation with STAI-S, in post examination).	32
	Santos et al. (2018), Portugal and Spain <sup>23</sup>	22 Oncological Patients	Pre and post-examination	STAI-S brief (scale 0–24); SEQ Physiologic parameters: o SBP and DBP (pre and post acquisition of the images)	STAI-S - Mean $\pm$ SD - 6.5 $\pm$ 4.0 SBP – median –129.0 DBP – median - 77.5  No statistically significant difference between STAI-S values and physiological measurements before and after examination	STAI-S - Mean $\pm$ SD - 7.1 $\pm$ 4.6 SBP – median –132.5 DBP – median - 77.5	–	27
	Goense et al. (2018), Netherlands <sup>24</sup>	27 Patients with newly diagnosed esophageal cancer	Post-examination (end of third PET/CT examination)	SRQ (with 5 points Likert scale);		Mean $\pm$ SD – 1.0 $\pm$ 0.2	Scan procedure: % of anxious patients o Discomfort due to body position in the scanner (52%). o Waiting time before scanning (19%); o Scan time (15%).	29
	Lorca et al. (2019), Spain <sup>25</sup>	54 Oncological Patients	Pre-examination Post-examination	STAI-S (scale 0–60) STAI-T (scale 0–60) -adHQ	STAI-S - 28.28 $\pm$ 8.08 STAI-T 16.09 $\pm$ 4.56 adHQ–6.03 $\pm$ 1.59	Not available		20
	Grilo at al., (2020), Portugal <sup>26</sup>	52 Oncological Patients	Pre-examination (on arrived at Department and prior to any information from the Health Professional); Post-examination (after the end of image acquisition).	STAI-S (scale 20-80) SEQ	STAI-S – Mean $\pm$ SD – 44.7 $\pm$ 10.0.  Statistically Significant difference between pre and post examination anxiety values.	STAI-S – Mean $\pm$ SD – 38.8 $\pm$ 11.3.	Concern with the result of the examination; Previous examination experience: Scan procedure: o Duration of the procedure and radiopharmaceutical injection. o Effects of radiation. (Significant moderate positive correlation with STAI-S pre examination); Radiation and examination duration explain 29.7% of the pre-examination anxiety	34
	Sun et al. (2020), China <sup>27</sup>	50 Oncological Patients	Post-examination (after scanning)	STAI-S (scale 20–80); STAI-T (scale 20–80); PEQ (based on the study Pettersen [24])		52% patients were anxious. STAI-S – Mean $\pm$ SD - 43.3 $\pm$ 10.5 STAI-T – Mean $\pm$ SD -40.7 $\pm$ 9.0		33

STAI-S - Spielberger State-Trait Anxiety Inventory – State; STAI-T - Spielberger State-Trait Anxiety Inventory – Trait; HADS - Hospital Anxiety Depression Scale; SEQ-Scan Experience Questionnaires; DBP - Diastolic Blood Pressure; SBP-Systolic Blood Pressure; SRQ – Self Report Questionnaire; adHQ-ad hoc questionnaire; PEQ – Patient Experience Questionnaire.



was used in study Sun et al. (2020).<sup>27</sup> In two studies,<sup>18,23</sup> physiological measures were also considered, apart from self-report instruments.

Regarding the studies that did not use STAI, Abreu et al. (2017)<sup>15</sup> used an Anxiety Subjective Thermometer and SEQ, the same questionnaire already identified in three studies<sup>14,23,26</sup> and Goense et al. (2018)<sup>24</sup> used a Self-Report Questionnaire (SRQ).

Concerning the analysis of anxiety experienced by patients at the various stages of the <sup>18</sup>F-FDG PET/CT, eight studies evaluated anxiety in pre-examination,<sup>7,14,15,18,23,25,26</sup> seven studies in post-examination<sup>14,15,18,23,24,26,27</sup> and five studies on both times.<sup>14,15,18,23,26</sup>

#### *Anxiety in pre-examination <sup>18</sup>F-FDG PET/CT*

Considering the studies that addressed the pre-examination time,<sup>7,14,15,18,23,25,26</sup> it was found that most patients felt anxiety. Within this context, three studies,<sup>7,14,18</sup> identified 67.5%, 59.9% and 82.7%, of pre-examination anxiety, respectively. In the study by Abreu et al. (2017)<sup>15</sup> the subjective perception of anxiety was  $6.4 \pm 2.7$  on a 10-point Likert scale; in the study of Elboga et al. (2015)<sup>22</sup> and Grilo et al. (2020),<sup>26</sup> the mean results found were  $40.4 \pm 8.5$  and  $44.7 \pm 10$ , respectively, for a total of 80 points (STAI-S) and in the study by Lorca et al. (2019),<sup>25</sup> the value was  $28.28 \pm 8.08$  for a total of 60 points (STAI-S). Finally, in the study by Santos et al. (2018),<sup>23</sup> a mean of  $6.5 \pm 4.0$  was found for a total of 24 points (STAI-S brief version).

#### *Anxiety in post-examination <sup>18</sup>F-FDG PET/CT*

Seven studies,<sup>14,15,18,23,24,26,27</sup> included in this review, studied post-examination anxiety. In six studies, moderate to high anxiety values were found.

In the studies of Abreu et al. (2017)<sup>15</sup> and Goense et al. (2018),<sup>24</sup> the subjective perception of anxiety was  $5.7 \pm 2.6$  on a 10-point Likert scale and  $1.0 \pm 0.2$  on a 5-point Likert scale, respectively; and in the studies of Grilo et al. (2020)<sup>26</sup> and Sun et al. (2020)<sup>27</sup>  $38.8 \pm 11.3$  and  $43.3 \pm 10.5$ , for a total of 80 points STAI-S, respectively. Moreover, in the study of Grilo et al. (2017),<sup>14</sup> mean anxiety values of  $33.9 \pm 4.2$  were obtained for a total of 60 points STAI-S. In study by Santos et al. (2018),<sup>23</sup> a mean of  $7.1 \pm 4.6$  was obtained for a total of 24 points (STAI-S brief version).

#### *Comparison of pre and post examination patient anxiety <sup>18</sup>F-FDG PET/CT*

Five studies assessed pre- and post-examination anxiety.<sup>14,15,18,23,26</sup> In three of these studies,<sup>15,18,26</sup> there was decreased anxiety levels in self-reported measures. In two of the five studies, in which self-reported measures were taken, physiological measures were also taken.<sup>18,23</sup> In the Vogel et al. study (2012),<sup>18</sup> there was a decrease in cortisol values in saliva and heart rate from pre-examination to post-examination. However, in the study of Santos et al. (2018)<sup>23</sup> no statistically significant differences in physiological measurements were found.

#### *Factors contributing to anxiety in <sup>18</sup>F-FDG PET/CT examination*

The main anxiety factors pointed out by the studies included in this review were:

- (1) patients clinical situation,<sup>7,22</sup> particular, staging,<sup>7</sup> detection of recurrent disease<sup>7</sup> or patients who are at a higher stage of the disease<sup>22</sup>;
- (2) the submission of the patients to the <sup>18</sup>F-FDG PET/CT for the first time<sup>7,18</sup>;

- (3) the scan procedure, linked to several causes: the temperature of uptake room,<sup>18</sup> body position in the scanner,<sup>14,24</sup> waiting time before scanning,<sup>24</sup> scan time,<sup>24,26</sup> radiopharmaceutical injection<sup>26</sup> and effects of radiation<sup>15,26</sup>;
- (4) the patient concerned with the examination result<sup>14,26</sup>; and
- (5) the gender of the patients<sup>7,15,32</sup>: in two studies, higher anxiety was detected in men, although at various stages. In Abreu et al. (2017)<sup>15</sup> men were more anxious in the post-examination and in the study by Pifarré et al. (2011)<sup>7</sup> they were more anxious in pre-examination. However, in Elboga et al. study (2015),<sup>22</sup> the women presented the highest levels of anxiety.

## Discussion

This systematic review updates current research on anxiety experiences and factors contributing to anxiety in oncological patients undergoing PET/CT scans with <sup>18</sup>F-FDG. To the best of our knowledge, no systematic review has been done in this area. Following rigorous literature research based on PRISMA, ten articles were included for review.

Considering anxiety assessment, the articles included presented various measures/instruments: SEQ and adHQ developed by studies authors, HADS, PEQ and STAI. The latter measuring instrument, STAI, was used in eight studies.<sup>7,14,18,23,25–27</sup> Both STAI, STAI-S and STAI-T have been included in four studies.<sup>7,22,25,27</sup> STAI-S was used in six studies<sup>7,14,22,25–27</sup>; however, only three of these studies<sup>22,26,27</sup> scored the scale according to the authors' instructions (minimum 20, maximum 80).<sup>29</sup> In three studies<sup>7,14,25</sup> they used a score from 0 to 3, obtaining a minimum of 0 and a maximum of 60 points. Finally, two studies<sup>18,23</sup> applied an STAI-S brief version with eight items and differed in the form of scale scores, (minimum 8, maximum 32 and minimum 0 to maximum 24 points, respectively). Indeed, the STAI scale, a standardised tool developed to assess anxiety in healthy adults, can assess anxiety in the medical context and patients diagnosed with cancer, as already described.<sup>29–33</sup>

In this systematic review, it was also found that anxiety was assessed in different time phases of the procedure: pre-examination,<sup>7,14,15,18,23,25,26</sup> post-examination<sup>14,15,18,23,24,26,27</sup> and in both.<sup>14,15,18,23,26</sup> In this analysis, most patients included in the studies samples show significant anxiety levels in different examination time phases.

In three of the studies that assessed anxiety at both times,<sup>14,18,26</sup> it was found that anxiety levels were higher in pre-examination, probably reflecting the initial anxiety related to the scan procedure and environment. Post examination anxiety levels were significantly lower, suggesting that most patients' anxiety is related to the imaging procedure itself. These results following Himms-Hagen findings.<sup>34</sup>

Regarding the main factors triggering anxiety, the patients' clinical situation<sup>7,22</sup> was identified. Having an oncologic disease involves facing an unexpected situation that generates significant changes in a person's life.<sup>7</sup> Several authors<sup>35–37</sup> have described feelings of uncertainty, insecurity, and anxiety about what might happen during the cancer course. Confirmation of the disease and demanding treatment means an interruption in daily life and leads patients to face many new and stressful situations.<sup>8</sup>

The first-time patients undergoing the <sup>18</sup>F-FDG PET/CT<sup>7,18</sup> and the scan procedure were other anxiety factors outlined in this review. Anxiety in patients with no previous experience in the examination seems to be associated with a lack of knowledge about the procedure dynamics. The scan procedure anxiety may be related to several causes, namely intravenous injection, waiting time between the radiopharmaceutical injection and image

acquisition, exam duration, positioning, the temperature of uptake room and possible radiation side effects.<sup>16,38</sup>

The lack of information about the <sup>18</sup>F-FDG PET/CT procedure leads many patients to search for information independently on the internet. Often, patients face technical nature information, challenging to understand and focuses on the examination's threatening aspects.<sup>38–40</sup> These results are consistent with another PET/CT study<sup>13</sup> not included in the present review.<sup>13</sup>

Finally, patients concern with the examination results was another anxiety factor found in this systematic review.<sup>14,26</sup> It seems that patients' uncertainty about the outcome of the examination and awareness that the outcome may determine future treatments, or the course of the disease prevent patients from reducing anxiety.<sup>14,15</sup> These results have already been corroborated by other studies.<sup>41,42</sup>

As for the analysis of anxiety, considering sociodemographic factors, it was only possible to obtain some results on the gender variable. However, some distinct results were identified in this systematic review. Two studies<sup>7,15</sup> found higher anxiety levels in men patients. Although at various stages of the procedure, Abreu et al. (2018)<sup>15</sup> in the post-examination, while Pifarré et al. (2011)<sup>7</sup> in the pre-examination. Elboga et al. (2015)<sup>22</sup> found higher anxiety levels in women. Further research is needed to explore the difference in anxiety between gender as there are controversies in the literature.<sup>43,44</sup>

#### Relevance for clinical practice

Although it is evident that more research is needed considering anxiety levels and factors associated with it, this review assist health professionals to provide more adjustable support to oncological patients who undergo PET/CT. When the patient arrives at the Nuclear Medicine Department healthcare professionals must pay significant attention to patients who examined for the first time. It is crucial to understand if the patient has searched for PET/CT information and personalized information clarifying all his doubts and myths, especially the radiation ones. Before the acquisition of images, the professionals' attention should be focused on patient positioning. It will be necessary that before starting the scan, a position is found where the patient can be relatively comfortable and without cold during the entire acquisition period.

#### Limitations

This systematic review includes studies with a relevant heterogeneity considering the sample size, the location of the primary tumour, the anxiety measures/instruments, and the anxiety assessment timing, that limits the generalization of the results. Also, regarding the geographical location of the studies included, it was found that most of them were conducted in four countries on the European continent<sup>7,14,15,18,22–26</sup> and one in Asia.<sup>27</sup> Finally considering anxiety instruments, using the STAI scale with different scales and scores made it challenging to compare results, especially on average anxiety values. Besides, not all studies have indicated their mean scoring criteria, making it difficult to interpret the results.

#### Conclusion

In conclusion, this review is the first analysing oncological patients' anxiety experience during PET/CT with <sup>18</sup>F-FDG. The ten studies reviewed here suggest that moderate to high levels of anxiety are present in most of the patients who undergo the examination. This review also highlights several factors related to the anxiety levels through different procedure moments, namely

clinical situation, first-time patients undergoing <sup>18</sup>F-FDG PET/CT, scanning procedure and concern with the examination result.

Future research, using robust study designs and including subjective and physiological, will be required to understand further anxiety experienced by adult oncological patients who undergo PET/CT with <sup>18</sup>F-FDG, in the pre-and post-examination phases. These research results will improve health professionals' selection of non-pharmacological strategies that are more adjustable to decrease patient anxiety levels.

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#### Conflict of interest

None.

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#### References

- Boellaard R, Delgado-Bolton R, Oyen WJG, Giammarile F, Tatsch K, Eschner W, et al. FDG PET/CT: EANM procedure guidelines for tumour imaging: version 2.0. *Eur J Nucl Med Mol Imag* 2015;**42**(2):328–54.
- Clinical Guidelines. *Oncology imaging policy. Version 1.0 effective. February 14, 2020. eviCore oncology imaging guidelines - effective 2/14/2020.*
- Lau J, Rousseau E, Kwon D, Lin K, Bénard F, Chen X. Insight into the development of PET radiopharmaceutical for oncology. *Cancers* 2020;**12**(5):1312.
- Food & Drug Administration. *Review of F-18 fluoro-2-deoxyglucose (F-18 FDG) positron emission tomography in the evaluation of malignancy - August 4, 1999.* <https://www.fda.gov/drugs/pharmaceutical-quality-resources/review-f-18-fluoro-2-deoxyglucose-f-18-fdg-positron-emission-tomography-evaluation-malignancy-august, 2021.> [Accessed 27 July 2020].
- Delbeke D, Coleman RE, Guiberteau MJ, Brown ML, Royal HD, Siegel BA, et al. Procedure guideline for tumor imaging with 18F-FDG PET/CT 1.0\*. *JNM (J Nucl Med)* 2006;**47**(5):885–95.
- Abreu C. *Dissertation, Escola Superior de Tecnologia da Saúde de Lisboa. Instituto Politécnico de Lisboa*; 2014.

7. Pifarré P, Simó M, Gispert JD, Pallarés MD, Plaza P, Martínez-Mirallés E. Diagnostic imaging studies: do they create anxiety? *Rev Española Med Nucl* 2011;**30**(6):346–50.
8. Grau A, Comas P, Suner R, Pelaez E, Sala L, Planas M. Evolution of anxiety and depression detected during hospitalization in an internal medicine service. *An Med Int* 2007;**24**:212e6.
9. Barlow DH. Unraveling the mysteries of anxiety and its disorders from the perspective of emotion theory. *Am Psychol* 2000;**55**(11):1247–63.
10. Sandman PM. *Responding to community outrage: strategies for effective risk communication*. American Industrial Hygiene Association; 2012. Published 1993, <http://psandman.com/media/RespondingtoCommunityOutrage.pdf>. [Accessed 27 July 2020].
11. Perry KN, Burgess M. *Communication in cancer care*. Oxford, U.K.: Blackwell Publishing; 2002.
12. Mathers SA, McKenzie GA, Robertson EM. A necessary evil: the experiences of men with prostate cancer undergoing imaging procedures. *Radiography* 2011;**17**:284–91. <https://doi.org/10.1016/j.radi.2011.06.005>.
13. Acuff SN, Bradley YC, Barlow P, Osborne DR. Reduction of patient anxiety in PET/CT imaging by improving communication between patient and technologist. *J Nucl Med Technol* 2014;**42**(3):211–7.
14. Grilo A, Vieira L, Carolino E, Oliveira C, Pacheco C, Castro M, et al. Anxiety in Cancer Patients during 18 F-FDG PET/CT Low Dose: a comparison of anxiety levels before and after imaging studies. *Nurs Res Pract* 2017;**30**:57495:9.
15. Abreu C, Grilo A, Lucena F, Carolino E. Oncological patient Anxiety in imaging studies: the PET/CT example. *J Canc Educ* 2017;**32**(4):820–6.
16. Bastiaannet E, Hoekstra-Weebers JE, Francken AB, Jager PL, Van Der Jagt EJ, Hoekstra HJ. Perception of burden experienced during diagnostic tests by melanoma patients with lymph node metastases. *Melanoma Res* 2009;**19**(1):36–41.
17. Rosenbaum SJ, Lind T, Antoch G, Bockisch A. False-positive FDG PET uptake—the role of PET/CT. *Eur Radiol* 2006;**16**:1054–65.
18. Vogel WV, Valdés Olmos RA, Tijs TJW, Gillies MF, van Elswijk G, Vogt J. Intervention to lower anxiety of 18F-FDG PET/CT patients by use of audiovisual imagery during the uptake phase before imaging. *J Nucl Med Technol* 2012;**40**(2):92–8.
19. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ* 2009;**339**. <https://doi.org/10.1136/bmj.b2700>.
20. RUSH University Medical Center (s. d). Doctor of nursing practice (DNP) guide. <https://rushu.libguides.com/dnp/pico> <https://rushu.libguides.com/dnp/pico>. Accessed July 27, 2020.
21. Hawker S, Payne S, Kerr C, Hardey M, Powell J. Appraising the evidence: reviewing disparate data systematically. *Qual Health Res* 2002;**12**(9):1284–99. <https://doi.org/10.1177/1049732302238251>.
22. Elboga U, Elboga G, Can C, Sahin E, Karaoglan H, Kalender E, et al. Assessment of procedure related anxiety and depression in oncologic patients before F-18 FDG PET-CT imaging. *J Psychiatr* 2015;**18**:1.
23. Santos A, Martins A, Sousa C, Vieira L, Grilo A, Carolino E, et al. Eficácia da música no controlo da ansiedade durante o exame de PET/TC. *Saúde Tecnol* 2018;**19**:12–9.
24. Goense L, Borggreve A, Heethuis SE, van Lier AL, van Hillegersberg R, Mook S, et al. Patient perspectives on repeated MRI and PET/CT examinations during neoadjuvant treatment of esophageal cancer. *Br J Radiol* 2018;**91**(1086). 20170710.
25. Lorca AM, Lorca MM, Criado J, Aguado R, Baños MC, Armesilla MD. Using mindfulness to reduce anxiety during PET/CT. *Mindfulness* 2019;**10**:1163–8.
26. Grilo A, Vieira L, Carolino E, Costa M, Galao S, Melo I, et al. Cancer patient experience in a nuclear medicine department: comparison between bone scintigraphy and 18F-FDG PET/CT. *J Nucl Med Technol* 2020;**48**(3):254–64.
27. Sun Y, Sun Y, Qin Y, Zhang Y, Yuan H, Yang Z. Virtual experience' as an intervention before a positron emission tomography/CT scan may ease patients' anxiety and improve image quality. *J Med Imaging Radiat Oncol* 2020;**64**:1–10. <https://doi.org/10.1111/1754-9485.13078>.
28. Pettersen KI, Veenstra M, Guldov B, Kolstad A. The patient experiences questionnaire: development, validity and reliability. *Int J Qual Health Care* 2004;**16**:453–63.
29. Spielberg CD, Gorsuch RL, Lushene RE. *Manual for the state/trait anxiety inventory*. Palo Alto (CA): Consulting Psychologists Press; 1983.
30. Fafouti M, Paparrigopoulos T, Zervas Y, Rabavilas A, Malamos N, Liappas I, et al. Depression, anxiety and general psychopathology in breast cancer patients: a cross-sectional control study. *In Vivo* 2010;**24**:803–10.
31. Mystakidou K, Tsilika E, Parpa E, Gogou P, Theodorakis P, Vlahos L. Self-efficacy beliefs and levels of anxiety in advanced cancer patients. *Eur J Canc Care* 2010;**9**:205–11.
32. Alacacioglu A, Binicier O, Gungor O, Oztop I, Dirioz M, Yilmaz U. Quality of life, anxiety, and depression in Turkish colorectal cancer patients. *Support Care Canc* 2008;**18**:417–21.
33. Sukegawa A, Miyagi E, Asai-Sato M, Saji H, Sugiura K, Matsumura T, et al. Anxiety and prevalence of psychiatric disorders among patients awaiting surgery for suspected ovarian cancer. *J Obstet Gynaecol Res* 2008;**34**:543–51.
34. Himms-Hagen J. Brown adipose tissue thermogenesis, energy balance, and obesity. *Can J Biochem Cell Biol* 1984;**62**:610–7.
35. Hefez A, Gaber LB, Arison Z, Robinson E. Anxiety in cancer patients – a pilot study. *J Psychiatr Relat Sci* 1982;**19**:303–13.
36. Sussman N. Reactions of patients to the diagnosis and treatment of cancer. *Anti Canc Drugs* 1995;(Suppl 1):4–8.
37. Klikovac T, Djurdjevic A. Psychological aspects of the cancer patient's education: thoughts, feelings, behavior and body reactions of patients faced with diagnosis of cancer. *J BUON* 2010;**15**:153–6.
38. Andersson C, Johansson B, Wassberg C, Johansson S, Sundin A, Ahlström H. Assessment of whether patients' knowledge, satisfaction, and experience regarding their <sup>18</sup>F-fluoride PET/CT examination affects image quality. *J Nucl Med Technol* 2016;**44**(1):21–5.
39. Andersson C, Johansson B, Wassberg C, Johansson S, Ahlström H, Wikehult B. Patient experience of an 18F-FDG PET/CT examination: need for improvements in patient care. *J Radiol Nurs* 2015;**34**:100–8.
40. Bowden DJ, Yap LC, Sheppard DG. Is the internet a suitable patient resource for information on common radiological investigations? Radiology-related information on the internet. *Acad Radiol* 2017;**24**:826–30.
41. Groves AM, Kayani I, Syed R, Gacinovic S, Nagabushan N, Ell PJ. Myocardial perfusion scintigraphy: patients' perception of benefit and risk. *Nucl Med Commun* 2004;**25**(12):1219–22.
42. Baun C, Vogsen M, Nielsen MK, Høiland-Carlson PF, Hildebrandt MG. Perspective of patients with metastatic breast cancer on electronic access to scan results: mixed methods study. *J Med Internet Res* 2020;**22**(2):e15723.
43. Nightingale JM, Murphy FJ, Blakeley C. I thought it was just an x-ray: a qualitative investigation of patient experience in cardiac SPECT-CT Imaging. *Nucl Med Commun* 2012;**33**(3):246–54.
44. Tornqvist E, Manasson A, E-M L, Hallström I. Impact of extended written information on patient anxiety and image motion artifacts during magnetic resonance imaging. *Acta Radiol* 2006;**47**:474–840.