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The Role of Positron Emission Tomography Imaging in Breast Implant Illness

Siham Azahaf, MD*
Karlinde A. Spit, MD*
Christel J.M. de Blok, MD, PhD*
Peter Bult, MD, PhD†
Prabath W.B. Nanayakkara, MD, PhD, FRCP*

Background: Explantation often alleviates symptoms in women with breast implant illness. However, persistent complaints in some cases may be linked to persistent silicone-induced inflammation from residual silicone particles. Positron emission tomography (PET) imaging could potentially detect this inflammation. This case series describes the PET findings in women with ongoing symptoms after explantation.

Methods: A retrospective review was performed of cases from the silicone outpatient clinic at the Amsterdam University Medical Centers, the Netherlands. All women underwent PET imaging due to persistent systemic symptoms after explantation (n = 17) or replacement (n = 1).

Results: Before PET imaging, silicone deposits were demonstrated in all 18 cases using ultrasound or magnetic resonance imaging. PET imaging revealed varying fluorodeoxyglucose avidity in axillary, parasternal, mediastinal, cervical, or supraclavicular lymph nodes and extranodal sites in all patients, up to 11 years after explantation. The median implantation time was 17 years, the average number of implant sets was 2, and the median time from explantation to PET was 2 years. In cases where biopsy was performed, silicone lymphadenitis with characteristic foreign body reaction was confirmed. The PET findings suggest that silicone residues can provoke inflammation even years after explantation. However, not all women with silicone residues may exhibit fluorodeoxyglucose-positive PET scans, indicating variability in susceptibility to silicone-induced inflammation.

Conclusions: PET imaging may be a useful diagnostic tool for detecting silicone-induced inflammation in patients with persistent complaints after explantation. However, given inherent limitations, further research is warranted to fully assess its potential diagnostic utility in breast implant illness. *(Plast Reconstr Surg Glob Open 2025; 13:e6458; doi: 10.1097/GOX.0000000000006458; Published online 16 January 2025.)*

INTRODUCTION

Breast augmentation is the most commonly performed cosmetic surgical procedure worldwide, particularly among young women 18–34 years of age.[1] However, the safety of breast implants has been a persistent topic of controversy. In the past few years, the debate on safety reignited due to the emergence of implant-related cancers, including breast implant-associated anaplastic large cell lymphoma (BIA-ALCL), breast implant-associated squamous cell carcinoma, and others, including sarcoma.[2] Consequently, a substantial increase of 55% in implant removal procedures was noted from 2018 to 2022.[1]

Moreover, recognition of a cluster of complaints reported by a subset of women with breast implants is increasing. This novel disease, termed breast implant illness (BII) among other nomenclatures, is a constellation of systemic and local complaints, including but not limited to debilitating fatigue, joint pain, axillary

*From the *Section General Internal Medicine, Department of Internal Medicine, Amsterdam Public Health Research Institute, Amsterdam University Medical Centers, Amsterdam, The Netherlands; and †Department of Pathology, Radboud University Medical Centre, Nijmegen, The Netherlands.*

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Drs. Azahaf and Spit contributed equally to this article.

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lymphadenopathy, and painful breasts.[3] Symptoms typically emerge 10 years after implantation.[3–5] We currently lack a biomarker for BII, leading to skepticism among physicians and complicating decision-making for patients considering removal of breast implants. At present, BII is approached as a "diagnosis per exclusionem," in a patient with the known cluster of symptoms.[2] The current gold standard treatment is surgical removal of the implants (explantation) leading to significant symptom improvement in more than 70% of women.[3,4,6] However, a subset of women do not experience relief, which could be due to comorbidities, an alternative diagnosis, or persistent inflammation from silicone residues.

BII is conjectured to be the result of silicone-induced inflammation in susceptible individuals.[7,8] Therefore, device failure leading to silicone leakage remains a pressing issue.[9] Silicone particles from the breast implants have the potential to migrate to nodal and distant body sites, inciting an inflammatory response.[10,11] This can happen when implants rupture or through implant "bleeding" from both the gel and shell.[10,12] Silicone migration as a cause of lymphadenopathy, first documented by Wintsch et al,[13] remains an underrecognized clinical entity among women with breast implants. This is due to the lack of standardized screening protocols and clinical management strategies. Interestingly, the potential link between silicone lymphadenopathy and BII has not been studied, leaving uncertainties regarding its implications for patients. Several case reports warn physicians of the similarities between silicone lymphadenopathy, (metastatic) cancer, and infectious diseases on positron emission tomography (PET) imaging.[14,15] Therefore, PET imaging may be a useful diagnostic tool in demonstrating silicone-induced inflammation in the context of BII.[14,16–18] This case series aimed to document PET scan findings in women who continue to experience systemic symptoms after explantation. This article is designed to explore possible patterns in PET imaging that could inform future research directions.

Takeaways

Question: Can silicone residues from silicone breast implants cause inflammation after the implants are removed?

Findings: Using positron emission tomography–computed tomography, we identified fluorodeoxyglucose-avid lymph nodes and other tissues with silicone residues in women with persistent complaints years after the surgical removal of the implants.

Meaning: Silicone residues may elicit inflammatory responses even years after the surgical removal of breast implants, potentially explaining persistent symptoms of breast implant illness. The role of positron emission tomography imaging in breast implant illness warrants further research.

METHODS

The Silicone Outpatient Clinic

This case series was conducted using data collected retrospectively from patients who visited the specialized BII outpatient clinic at Amsterdam University Medical Centers in the Netherlands. Ethical approval for the study was obtained from the ethical review board of the Amsterdam UMC (reference number: 2024.0079).

At this clinic, we evaluate and treat women with systemic complaints potentially related to breast implants. Patients are typically referred by general practitioners, plastic surgeons, or other specialists, whereas their implants are still in situ. After excluding alternative diagnoses, patients with a strong suspicion of BII are referred for explantation by a plastic surgeon. Symptom evaluation is conducted 6–12 months after explantation. In addition, some patients are referred to our clinic postexplantation due to persistent symptoms, and occasionally, patients are referred after undergoing diagnostic tests, including PET scans initiated by other specialists who suspected malignancies but found silicone deposits on biopsy.

Patient Selection

For this series, we included women with a high suspicion of BII, a history of implant rupture and/or before radiological identification of lymphadenopathy with silicone deposits, and persistent systemic complaints after explantation. All included patients underwent PET–computed tomography (CT) scans between 2022 and 2024. One patient decided to replace her implants against medical advice and presented with persistent complaints.

PET-CT scans were performed to identify fluorodeoxyglucose (FDG)-avid lymph nodes and to rule out other potential causes for persistent symptoms, such as malignancies. Biopsies of lymph nodes were conducted when clinically indicated. Clinical, radiological, and pathological data were collected from medical records.

Statistical Analysis

Continuous variables, such as time from explantation to PET-CT and implant duration, are presented as medians with interquartile ranges. Categorical variables, including imaging findings and biopsy results, are summarized as frequencies and percentages.

RESULTS

Clinical Features

A total of 17 women with persistent complaints postexplantation, and in 1 case postreplacement, who underwent PET-CT scans in 2022–2024, are presented. An overview of the demographics is presented in Table 1. Fourteen women were referred to our clinic due to persistent complaints after explantation. In 5 of these patients, PET scans were already performed by other specialists. In 4 of these 5 patients, lymph node biopsies were performed to rule out malignancy, revealing silicone lymphadenitis. The remaining 4 women were diagnosed with BII in our clinic, referred to a plastic surgeon for explantation, and returned with persistent complaints 6–12 months later. All women had a history of implant rupture and experienced

Table 1. Demographic and Clinical Features

Patient Characteristics	Patients, N (%)
Age (range), y	52 (37–64)
Implantation time (range), y	17 (5–39)
Reason for implant	
Augmentation	17 (94)
Reconstruction	1 (6)
Breast implants details	
Average no. sets (total)	2 (36)
Unilateral	1
Bilateral	17
Brands	
Allergan	10
PIP	5
Eurosilicone	4
Monobloc hydrogel	1
Saline	1
Motiva	1
Unknown	14
Time implant removal to PET (range), y*	2 (0.5–11)
Smoking	
Current	4 (22)
Former	8 (44)
Never	6 (33)
Allergies	12 (67)
Local symptoms	15 (83)
Systemic symptoms	
Fatigue	18 (100)
Joint pain	18 (100)
Myalgia	17 (94)
Sicca complaints	12 (67)
Night sweats	10 (56)
Neurological symptoms (eg, brain fog)	10 (56)
Rashes	10 (56)
Flu-like feeling	9 (50)
Morning stiffness	8 (44)
Weight loss	8 (44)
Hair loss	7 (39)
Sleeping disturbances	6 (33)
Palpitations	6 (33)
Dyspnea	5 (28)

*Replacement: n = 1.
PIP, poly implant prothèse.

symptoms fitting the description of BII. The majority of women experienced concomitant local complaints. Laboratory results showed no elevated inflammatory markers. Three women tested positive for antinuclear antibodies using the indirect immunofluorescence assay.

Imaging Findings

All women underwent 1 or more imaging studies including mammary and axillary ultrasound (US) or breast magnetic resonance imaging (MRI) (Table 2). The majority underwent these studies before explantation. In women who presented to our clinic years after explantation, a US was performed to assess the presence of silicone in the axillary lymph nodes or mammary tissue. All USs showed signs of axillary silicone depositions, defined as the "snowstorm sign."[19] Furthermore, US examination identified extracapsular silicone in mammary tissue in 6 women. MRI was performed in 11 women before explantation, of whom only 9 showed signs of axillary silicone depositions. However, MRI additionally identified silicone depositions in parasternal, mediastinal, and supraclavicular lymph nodes. MRI detected intramammary silicone depositions in 4 women, as the remaining 2 identified by US did not undergo an MRI. MRI further identified seroma and silicone depositions in or near the pectoral muscle.

Months to years after explantation, PET imaging, often in combination with chest CT, was performed in all women (Table 2). All women showed F-18 FDG-avid axillary lymph nodes corresponding to the findings on either or both US or MRI. (**See figure, Supplemental Digital Content 1,** which displays PET imaging revealing FDG avidity of silicone residues. A, PET-CT scan 2 years postexplantation revealing extensive FDG-avid lymphadenopathy in the left axilla, extending to the high axilla and retropectoral regions. For example, an enlarged lymph node with a short-axis diameter of 10 mm [A]. In addition, several FDG-avid nonenlarged lymph nodes are observed in the right axilla. Also shown is an enlarged retropectoral lymph node with a short-axis diameter of 15 mm [B]. Implantation time: 23 years. B, PET-CT imaging in a patient reveals multiple enlarged lymph nodes with intense FDG uptake [arrow], corresponding to silicone lymphadenopathy observed on MRI [arrow]. The patient was awaiting explantation. Implantation time: 35 years. C, PET-CT imaging 2 years postexplantation in a female patient shows intense FDG uptake intramammary [arrows] in areas corresponding to silicone depositions observed on MRI [arrows]. Implantation time: 21 years. A,

Table 2. Silicone-induced Lymph Nodes and Extranodal Sites Based on Clinical, Radiological, or Pathological Findings

		Radiology, N (%)			
	Physical Examination, N (%), n = 18 (%)	US (n = 17)	MRI (n = 11)	PET-CT (n = 18)	Pathology, N (n = 9)
Lymph nodes					
Axillary	11 (61)	17 (100)	9 (82)	18 (100)	6
Parasternal	n.a.	n.p.	3 (27)	9 (50)	1
Mediastinal	n.a.	n.p.	1 (9)	2 (11)	n.p.
Cervical	2 (11)	2 (12)	n.p.	2 (11)	1
Supraclavicular	1 (6)	1 (6)	1 (9)	4 (22)	n.p.
Extranodal sites					
Intramammary	n.a.	6 (35)	4 (36)	7 (39)	n.p.
Pectoral muscle	n.a.	n.p.	2 (18)	12 (67)	n.p.
Seroma	0	0	2 (18)	2 (11)	1

n.a., not applicable; n.p., not performed.

PET-CT scan 2 years postexplantation revealing extensive FDG-avid lymphadenopathy in the left axilla, extending to the high axilla and retropectoral regions. For example, an enlarged lymph node with a short-axis diameter of 10 mm [A]. In addition, several FDG-avid nonenlarged lymph nodes are observed in the right axilla. Also shown is an enlarged retropectoral lymph node with a short-axis diameter of 15 mm [B]. Implantation time: 23 years, **http://links.lww.com/PRSGO/D789**.)

The time period from implant removal to PET-positive silicone lymphadenitis ranged from 5 months to 11 years. In addition, PET imaging showed FDG avidity in parasternal, mediastinal, cervical, and supraclavicular lymph nodes. Furthermore, other FDG-positive areas included intramammary tissue and pectoral muscle **(Supplemental Digital Content 1, http://links.lww.com/PRSGO/D789**). None of the women had comorbidities that could account for the observed PET abnormalities. (**See table, Supplemental Digital Content 2,** which displays the overview of comorbidities of cases, **http://links.lww.com/PRSGO/D790**.)

Cervical Lymphadenopathy

Two cases of cervical lymphadenopathy with silicone depositions were observed. The first case involved a patient with 14-year monobloc implants and no relevant medical history, who developed BII and cervical lymphadenopathy 9 years postimplantation. She visited her general practitioner after she noticed cervical swollen lymph nodes. A US and biopsy revealed silicone foreign body reaction. Chest imaging detected a ruptured left implant and explantation led to minimal symptom improvement. Subsequent imaging, performed 8 months later, revealed persistent FDG-positive cervical lymphadenitis involving at least 9 lymph nodes in levels IV and Vb on the left side, along with affected axillary and parasternal lymph nodes and FDG uptake subpectoral. Blood tests remained within normal limits. In the second case, a patient with unidentified brand implants for 33 years and no medical history developed BII symptoms 15 years postimplantation, accompanied by positive antinuclear antibodies and anticentromere antibodies. Despite clinical signs of systemic sclerosis, diagnostic criteria were not met. The patient chose implant replacement against medical advice. A PET scan demonstrated FDG-positive cervical and axillary lymph nodes, along with activity in the prepectoral area surrounding the implants.

Pathology

Histopathologic examination was conducted in 9 women, involving lymph node excision in 3 women, core needle biopsy in 4 women, and fine needle cytological aspiration in 2 women. Silicone lymphadenitis was confirmed in all cases. Silicone lymphadenitis typically presents with features of a foreign body reaction, with macrophages, intracytoplasmic silicone material, and foreign body type multinucleated giant cells. The macrophages may seem foamy with optically empty appearing vacuoles. However, with large magnification with light microscopy, the intracellular vacuoles exhibit amorphous, glassy, nonbirefringent material, consistent with silicone material. Also, macrophages may contain gray/black granular pigment. Silicone droplets can also be seen within the lymphoid tissue without obvious histiocytic reaction. Besides lymphocytes, the accompanying infiltrate may also include eosinophilic granulocytes and plasma cells. (**See figure, Supplemental Digital Content 3**, which displays [A] hematoxylin and eosin staining [×550 magnification] of a hot lymph node depicted in Supplemental Figure 1A, Supplemental Digital Content 1. Description: In a background of small lymphocytes and some eosinophilic granulocytes [some eosinophilic granulocytes are indicated with small arrows], multiple partly multinucleated, macrophages are seen with eosinophilic and vacuolated cytoplasm. De vacuoles contain glassy material consistent with silicone material [some intracytoplasmic silicone droplets are indicated with arrowheads]. Also, large droplets of glassy/silicone material without obvious histiocytic reaction are seen [some are indicated with large arrows]. B, Modified Oil-Red-O staining [MORO] [×550 magnification] of a lymph node, the same area as in Supplemental Figure 2A. The vacuoles in the macrophages [see also Supplemental Fig. 1A, Supplemental Digital Content 1] stain bright red in the MORO staining, confirming the presence of silicone material. Images are from a patient with 1 set of allergan implants and an implantation time of 8 years. A PET-CT performed 17 mo after explantation revealed FDG avidity of the axillary, mediastinal, and parasternal lymph nodes. Furthermore, activity was observed behind the pectoral muscle, **http://links.lww.com/PRSGO/D791**.) (**See figure, Supplemental Digital Content 4,** which displays [A] hematoxylin and eosin staining [×550 magnification] of a lymph node. In a background of small lymphocytes, multiple macrophages are seen with clear and vacuolated cytoplasm and gray/black granular pigment [some macrophages are indicated with arrowheads]. The vacuoles contain glassy material consistent with silicone material. B, MORO staining [×550 magnification] of a lymph node, the same area as in Supplemental Figure 3A. The vacuoles in the macrophages [see also Supplemental Figure 2A, Supplemental Digital Content 3] stain bright red in the MORO staining, confirming the presence of silicone material, **http://links.lww.com/PRSGO/D792**.)

The MORO staining can be used to confirm or detect the presence of silicone material (**Supplemental Digital Contents 3 and 4, http://links.lww.com/PRSGO/D791**, **http://links.lww.com/PRSGO/D792**.)[20–22] Cytological analysis of seroma fluid was performed in 1 patient to rule out BIA-ALCL.

DISCUSSION

In this case series, we presented the findings from women, which demonstrated silicone residues and persistent systemic symptoms postexplantation, and in 1 case postreplacement, who underwent PET imaging. PET imaging revealed silicone-induced lymphadenopathy and other hypermetabolic areas indicative of silicone-induced inflammation. These findings were corroborated by other

imaging modalities and histopathologic examination. Although it has been argued that silicone lymphadenopathy is merely a deposition without clinical significance, these findings suggest that silicone residues provoke an inflammatory response in susceptible women, resulting in chronic symptoms, as demonstrated by positive PET scans up to 11 years postexplantation.[17]

Similar PET abnormalities have been described in patients with free silicone injections.[23] The medical community has strongly advised against the use of free liquid silicone injections, due to serious adverse effects of silicone migration such as granuloma formation, recurrent cellulitis-like reactions, acute respiratory distress syndrome, and even death.[24–26] Silicone leakage from breast implants shows similar clinical presentations evidenced by reports on silicone-related scleroderma-like syndrome, chronic pulmonary silicone embolism syndrome, acute respiratory distress syndrome, pneumonitis, and granulomatous disease such as sarcoidosis.[10,27–30] Although the dissemination of silicone mainly presents through lymphatic pathways, hematogenous spread has also been reported. Montemurro et al[11] reported a case of ocular muscle palsy due to orbital silicone migration. They discovered a silicone granuloma in the right carotid artery of a patient with a ruptured left-sided breast implant. Although such reports seem rare, silicone-induced disease is easily overlooked and thus rarely included in any differential diagnosis.[10] The similarities between extensive silicone leakage from breast implants and free silicone injections are suggestive of a dose–response relationship to silicone, where the dose of silicone leakage may be associated with the severity of symptoms in susceptible patients. The variability in intensity and affected areas may account for the heterogeneity and intensity of BII symptoms in affected women. Persisting chest pain after explantation, for example, may partially be explained by silicone-induced inflammation in the pectoral muscle reflected on PET imaging.[31]

Not all women with silicone breast implants, silicone migration, and/or silicone lymphadenopathy have positive PET scans, suggesting susceptibility and potentially explaining the variability in symptom manifestation in women with proven silicone residues. Similar PET findings were described by Bauer et al,[14] who reported clinical correlates in a case series of 18 women with silicone lymphadenopathy. Sixteen patients were symptomatic and in 5 of the 18 patients, PET scans were performed, demonstrating positive results in only 3 patients. However, comprehensive subgroup analysis in women with or without complaints of BII and with or without silicone migration is warranted.

A few studies have linked ruptured silicone breast implants to systemic symptoms, supporting the conjecture of silicone-induced inflammation in BII. A study conducted by the US Food & Drug Administration found women with extracapsular silicone leakage to be 2.8 and 2.7 times more likely to report fibromyalgia and other connective tissue diseases, respectively.[32] Furthermore, another study found women with ruptured implants to report more symptoms of chronic fatigue syndrome compared with women with intact implants and controls.[33] To mitigate these effects, the US Food & Drug Administration advises women to pre-emptively screen for silent ruptures and undergo preventive replacements.[34] Although MRI is the golden standard for detecting implant ruptures, US has shown similar efficacy and may be more sensitive in detecting axillary silicone deposits.[35] However, our findings suggest that PET imaging is the most sensitive in mapping areas of silicone-induced inflammation.[36,37]

One might argue that the PET imaging merely reflects silicone's capacity to provoke a nonspecific foreign body reaction. However, the presence of adaptive immune cells in capsules challenges this notion. Furthermore, studies have shown that silicone can induce a potent T cell–mediated immune response.[38] This is not uncommon, as recognized host responses to foreign bodies include complement activation, delayed hypersensitivity, and adaptive immune cell responses.[8,39,40] In a typical foreign body reaction, the goal is to isolate the foreign body by the formation of a thin fibrous capsule. The foreign body reaction remains active until the implant is destroyed or removed, and the capsule remains a living tissue.[41] Although the chronic state of the foreign body reaction causes a lower grade of inflammation, implants continue to interact with surrounding tissue, causing damage and potential further inflammation in the presence of triggers, such as leakage.[39]

A proposed hypothesis for silicone-induced inflammation may be as follows: The presence and extent of silicone leakage could overwhelm the immune system of a susceptible subject due to the failed attempt of macrophages to eliminate the large foreign body and resolve inflammation. Macrophages may undergo unprogrammed cell death, releasing their content. Activated lymphocytes may target the silicone itself, as well as composite neoepitopes, cryptic epitopes, or modified self-proteins, leading to systemic disease in women with breast implants.[38] The presence of foreign body multinucleated giant cells (FBGCs) supports this conjecture. FBGCs form through the fusion of macrophages and digest foreign material that is too large for phagocytic uptake by a single macrophage. The accumulation of FBGCs leads to the formation of foreign body granulomas, as described in women with silicone breast implants (siliconoma).[15,42] It has been speculated that the formation of FBGCs is an attempt to avoid apoptosis.[43] This process has been described by Henson[44] as frustrated phagocytosis. Macrophages and foreign body giant cells release mediators of degradation such as reactive oxygen intermediates, degradative enzymes, and acids which harm implant integrity.[44,45] The variability in inflammation, FDG avidity, and systemic symptoms may reflect this highly complex and dynamic process.

The exact mechanism of silicone leakage and dispersion within the body remains unclear. Organosilicon compounds may exist in various forms, with some potentially phagocytized by immune cells.[10] The diversity of implants, each with unique physicochemical properties and proprietary formulations for both the gel and shell, complicates the matter. Moreover, the impact of biodegradation on the composition of these materials is not fully understood, and different organosilicon compounds trigger distinct molecular and cellular interactions within the human body. It could be hypothesized that systemic adverse reactions may be reversible by explantation of the breast implants within a certain

timeframe but may become irreversible beyond a critical threshold. Two studies reported greater improvement of BII symptoms when explantation is performed within 10 years postimplantation.[3,46] Furthermore, a recent study found grade IV (severe) capsular contracture to be correlated with an increased amount of silicone content in the capsules, corroborating silicone-induced inflammation and supporting the dose–response relationship.[22] However, not all women with breast implants experience symptoms, regardless of rupture status, which suggests variability in individual susceptibility.

Silicone lymphadenopathy and/or migration is regarded a rare complication. However, the absence of routine imaging for women with breast implants suggests that it may be underdiagnosed.[14,17,47] There has been a notable lack of follow-up studies examining the potential risks of silicone residues and their association with adverse health effects. Evidence-based strategies to guide clinical management practices are lacking, leading to significant apprehension among patients fearing the risk of cancer.[48] To our current knowledge, 1 case of axillary occurring BIA-ALCL has been described in a patient 2 years after explantation.[49] Surgical resection of siliconomas or silicone lymphadenopathy is not recommended due to associated risks, and no treatment exists to filter silicone from the body. Suppressive therapy with immunomodulators has demonstrated promising outcomes in cases of silicone-induced inflammation resulting from silicone injections.[50] However, the effectiveness of immunomodulators in treating silicone-induced inflammation related to breast implants has not been investigated through clinical trials.

Despite the inherent limitations of this case series, including selection bias due to referral to a specialized silicone outpatient clinic, the lack of a control group, and the small sample size, our findings suggest that PET imaging may offer valuable insights into persistent complaints experienced by women after explantation. The observed FDG-avid lymph nodes and areas corresponding to silicone presence suggest that PET imaging could be a useful tool for identifying silicone-induced inflammation. However, these results are preliminary, and further research is essential to validate these observations, address the limitations, and comprehensively assess the diagnostic utility of PET scanning in the context of BII.

Prabath W.B. Nanayakkara, MD, PhD, FRCP
Section General Internal Medicine
Department of Internal Medicine
Amsterdam Public Health Research Institute
Amsterdam University Medical Centers
Location VUmc
De Boelelaan 1118
1081 HZ, Amsterdam, The Netherlands
E-mail: p.nanayakkara@amsterdamumc.nl

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