Role of Multimodality for the Diagnosis of Thrombosis at Late Follow-up of Patients Selected for TAVI: Review of a Case Series

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Introduction

The first transcatheter aortic valve implantation (TAVI) was performed by Alan Cribier in France in 2002 and the technique was introduced in Brazil in 2008. Since then, this modality has been consolidated and many patients have been approached using this technique. After more than 10 years of the first TAVI in Brazil, an increasing number of late complications appear in the cardiovascular imaging laboratory, with challenging anatomical and functional aspects in daily practice. Late thrombosis of aortic endoprosthesis may be one of the causes of dysfunction in the follow-up after TAVI. This clinical entity can assume a complex profile for accurate diagnosis and proper patient management, since it can have a variable presentation, ranging from subclinical leaflet thrombosis to limiting symptoms related to heart failure.[1] Transesophageal echocardiography (TEE), the additional resource of 3D echocardiography and high-resolution computed tomography (CT) play a complementary role in the diagnosis of this etiology through anatomical valve reconstruction with evidence of hypoattenuated leaflet thickening (HALT) with or without hypoattenuation affecting motion (HAM) of one or more prosthetic valve leaflets.[2,3] The risk of embolic events after diagnosis of leaflet thrombosis is still uncertain, especially for the central nervous system.[4,5] This case series presents two illustrative reports of aortic endoprostheses with high gradients and complementary aspects of the multimodality that direct the etiology to the diagnosis of late prosthesis thrombosis.

Case report

Case 1

Female patient, 87 years old, with stable coronary artery disease (CAD), history of coronary angioplasty and severe aortic stenosis, who underwent TAVI and definitive pacemaker implantation in 2019, was admitted in June/2022 due to chest pain. An electrocardiogram revealed no acute ischemic abnormalities and normal myocardial necrosis markers. The transthoracic echocardiogram (TTE) showed aortic valve with high gradients, mean of 43 mmHg, differing from the last test performed in 2021, and transesophageal echocardiogram (TEE) showed leaflet thickening with significant motion hypoattenuation of two of its mobile elements, suggestive of prosthesis thrombosis, with effective flow orifice estimated by 3D planimetry and 3D continuity equation to be 0.73 cm^2 and 0.48 cm^2/m^2, indexed by the body surface (Figures 2 and 3).[6] CT revealed advanced-grade HALT in the three leaflets: leaflet equivalent to that of the left coronary artery, involvement greater than 75% (grade 4); leaflet equivalent to that of the right coronary artery, involvement greater than 75% (grade 4). Full anticoagulation therapy was initiated and presented good evolution. The patient was discharged in June/2022, clinically stable and asymptomatic (Figures 1, 2, 3 and 4) for outpatient follow-up.

Case 2

Male patient, 70 years old, hypertensive, with virus C parenchymal liver disease and thrombocytopenia, bicuspid aortic valve with a history of TAVI five years prior and recent history of leaflet thrombosis with severe aortic stenosis, was taking Clopidogrel and direct oral anticoagulants (DOAC). The patient was hospitalized in June/22 with acute respiratory distress associated with cough and hemoptysis. Underwent CT angiography of the chest with negative result for pulmonary thromboembolism and a pattern suggestive of alveolar hemorrhage. During this hospitalization, a new transthoracic echocardiogram was performed with evidence of persistently high gradients of the aortic endoprosthesis (maximum: 50 mmHg and mean: 28 mmHg), with HALT improvement on CT. The patient was discharged after clinical compensation, stable and, due to the high risk of bleeding, was maintained without anticoagulation (Figure 5).

Discussion

Transcatheter aortic valve replacement is a safe treatment and not inferior to conventional surgery for patients with severe symptomatic aortic stenosis and intermediate to high surgical risk.[7,8] With the national experience in the long-term follow-up of patients undergoing TAVI, there is an increasing number of cases of prosthetic stenosis with increased gradients and transvalvular velocities. In these situations, transthoracic echocardiogram can support the screening and identification of high gradients, however, it has a limited role in the etiological investigation.

Keywords

Multimodality; Prosthesis thrombosis; Transcatheter Aortic Valve Replacement

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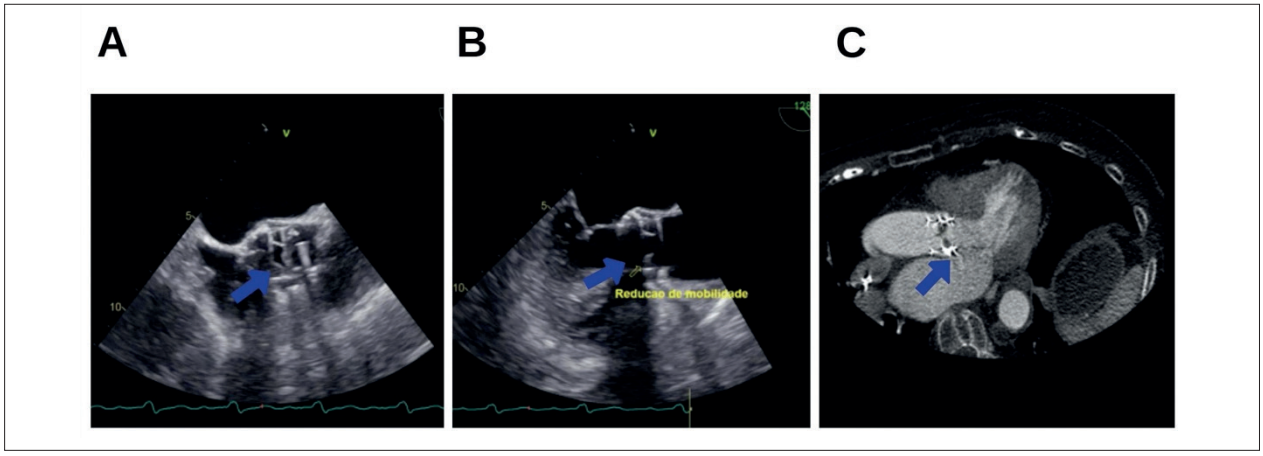

Figure 1 – *Images suggesting prosthesis thrombosis on TEE and cardiac CT. Reduced motion A and B: TEE at 45o and 130 o with evidence of leaflet thickening and reduced motion, respectively. C: HALT areas on cardiac CT.*

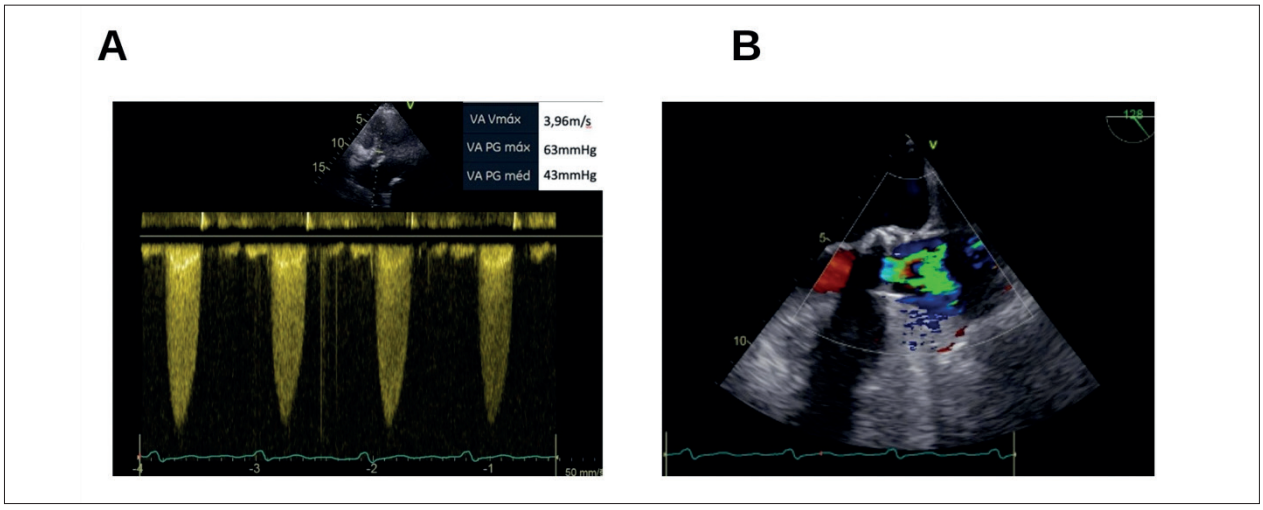

Figure 2 – *Echocardiographic findings of endoprosthesis dysfunction. A: High mean transprosthetic gradient at aortic position on transthoracic echocardiogram. B: TEE at 130o showing left ventricular outflow tract and aliasing on color Doppler flow through the endoprosthesis.*

Aortic endoprosthesis valve dysfunction is defined by transthoracic echocardiogram when there is a mean transvalvular gradient greater than 20 mmHg or greater than 50% of the previous mean baseline gradient.[2] Transesophageal echocardiography may have sensitivity comparable to cardiac CT in identifying signs of thrombosis, such as reduced leaflet motion, leaflet thickening, or even the identification of thrombi, especially in patients at increased risk of contrast nephropathy, which may contribute to the identification of the mechanism of prosthetic dysfunction.[2]

In this context, TEE can provide additional inputs in the evaluation of prosthesis dysfunction in the late follow-up of these patients. Real-time 3D complementation can be used in the evaluation of differential diagnoses of endoprosthesis dysfunction, especially for identifying images suggestive of endocarditis, mismatch, pannus and ascending aorta pathologies.

CT plays a crucial role in the complementary evaluation for the accurate diagnosis of post-TAVI prosthesis thrombosis. This test can identify prosthesis thrombosis through morphological criteria with a finding of HALT that may be associated with HAM, and the possibility of assessing the thrombotic load, a parameter that has been correlated with adverse clinical outcomes.[4,9,10] HALT can be classified according to the extent of leaflet involvement as <25%, 25–50%, 50–75% or >75%, with this assessment being performed on CT diastolic reconstructions (Figure 6). However, the presence of HALT is observed at similar rates for transcatheter and surgical prosthetic valves.[5,11]

Some elements are recognized as factors that may function as independent predictors of evolution to late thrombosis in the follow-up after TAVI. Some of these characteristics are based on clinical attributes, such as atrial fibrillation, chronic obstructive pulmonary disease, male gender, absence of postoperative treatment with

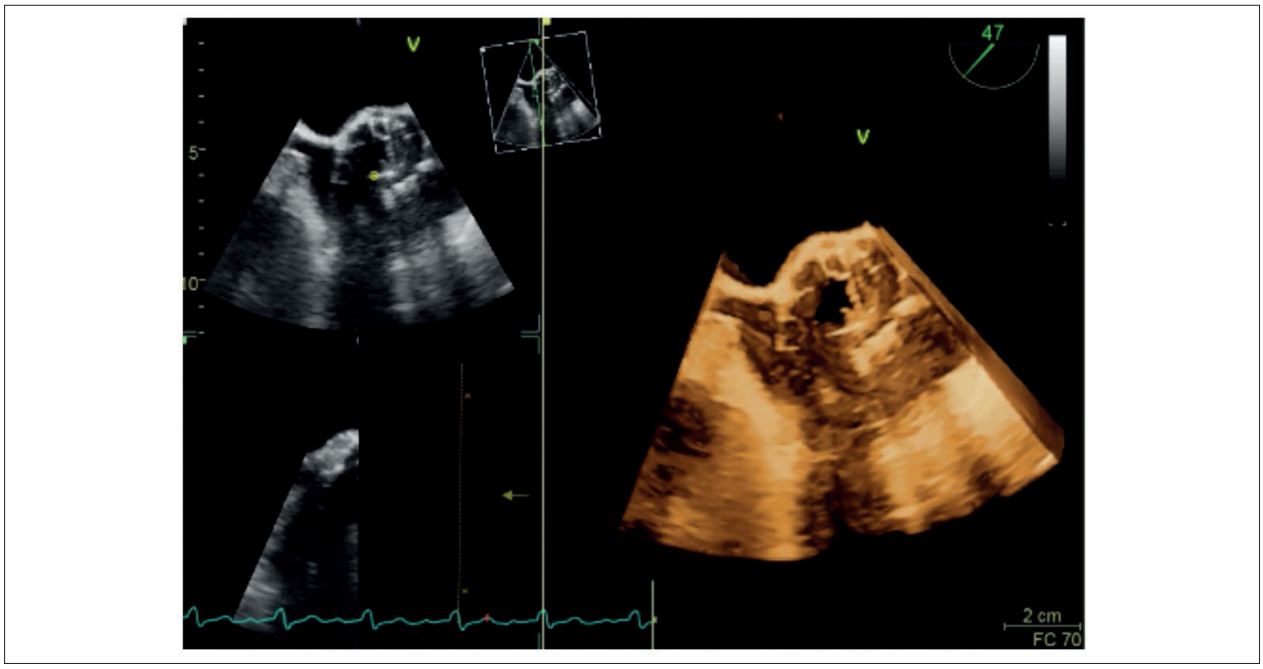

Figure 3 – *3D reconstruction of the aortic endoprosthesis. TEE at 45o with leaflet thickening and reduced motion (indicated by the arrow) with no images suggesting endocarditis.*

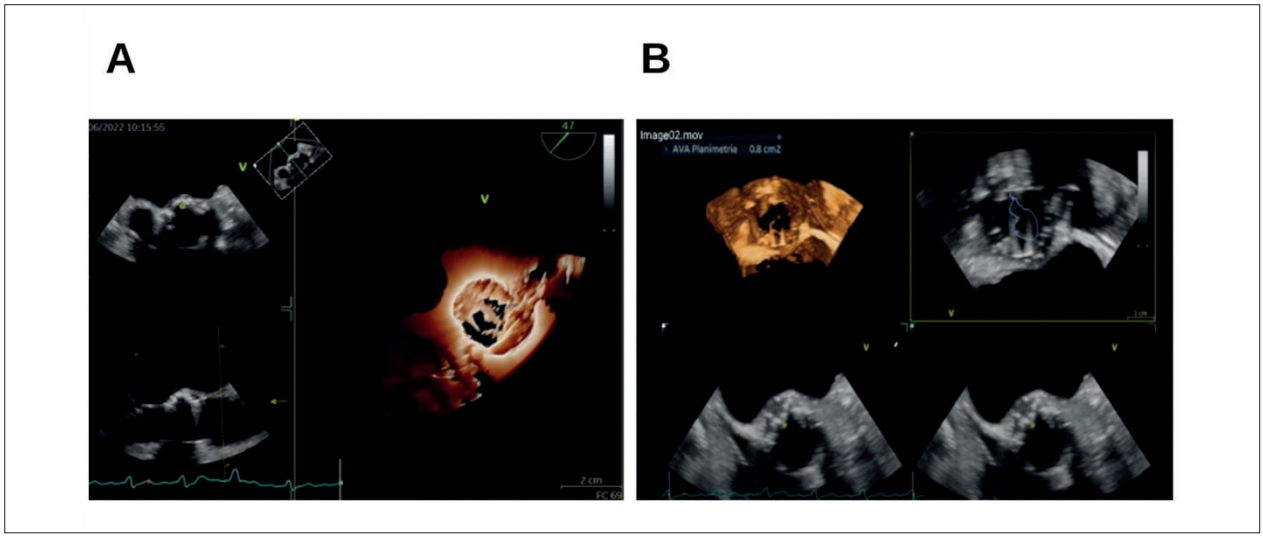

Figure 4 – *3D reconstruction of the aortic endoprosthesis. A: TEE at 45o with 3D reconstruction of the aortic endoprosthesis. B: estimation of effective flow orifice through 3D planimetry.*

antiplatelet agents, obesity and active smoking. Other factors are related to the intra-procedure, such as the smaller diameter of the implanted prosthesis, the supra-annular device implantation, balloon under-expansion and valve-in-valve procedure.[10,12,13] As for imaging methods, reduced left ventricular ejection fraction and paravalvular leak are strong predictors that may indicate a higher risk of thrombosis of an evolutionary prosthesis. Some studies describe a two-fold increase in late thrombosis in patients with at least mild leak.[11]

Symptomatic thrombosis of aortic valve endoprosthesis leaflets is rare, representing about 0.6 to 2.8% of reported cases,[8] contrasting with incidental finding in about 15–40% of subclinical thrombosis with evidence of HALT on cardiac CT, with a potential association with cerebrovascular events.[5,7,9] Optimal antithrombotic therapy is still the focus of clinical trials, with current guidelines recommending dual antiplatelet therapy (DAPT) for three to six months after TAVI and data regarding safety and longevity suggesting good durability in five years.[1,7] However, some studies suggest that subclinical

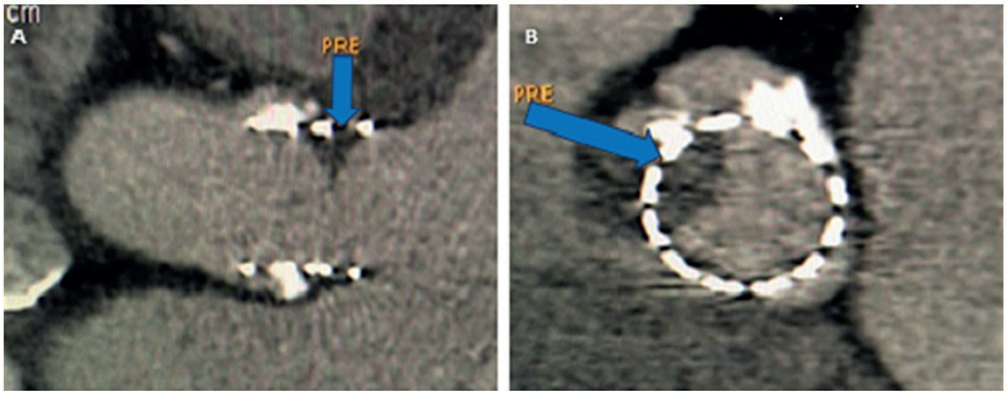

Figure 5 – *Multiplanar tomographic reconstruction A and B: long and short axis, respectively, showing non-coronary leaflet with grade 4 HALT. PRE: HALT before anticoagulation.*

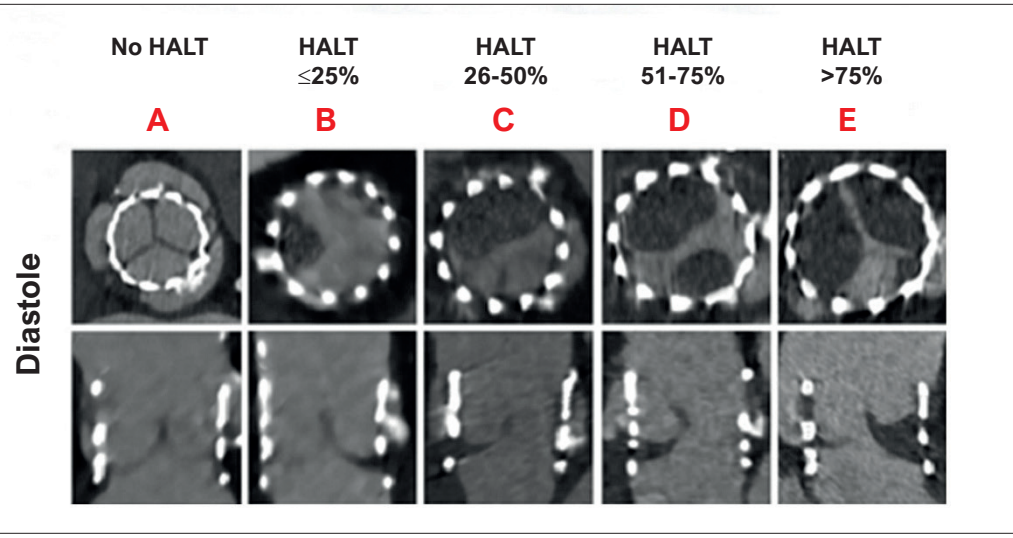

Figure 6 – *HALT classification through diastolic reconstruction by CT, cross-sectional and longitudinal axis. A: no leaflet involvement. B: leaflet involvement at ≤25%, C: 26–50%. D: 51–75%. E: >75%. HALT: hypoattenuated leaflet thickening.*

thrombosis is more common in those who did not receive anticoagulation, so that, after discontinuing DOAC, CT can reveal HALT in a variable degree, revealing its dynamic nature due to the potential of spontaneous progression or regression, even in asymptomatic patients.[1,5,7,11] However, the GALILEO trial demonstrated that the use of routine oral anticoagulants should be avoided after TAVI in order to prevent subclinical structural alterations, with well-established indications in view of the increased risk of death and bleeding.[14]

The follow-up of patients diagnosed with TAVI thrombosis and establishment of the indicated therapy are not well established in the literature. This follow-up is usually carried out systematically and periodically using serial transthoracic echocardiography with comparative assessment of transprosthetic systolic gradients and velocities, associated with complementary CT imaging to assess the quantitative reduction in leaflet thickening and improvement of leaflet motion[14] (Figure 7).

Conclusion

Aortic valve replacement with endoprostheses for the treatment of symptomatic aortic stenosis has raised the issue of long-term safety and longevity of the endoprosthesis. The use of multimodality in the follow-up of these patients has identified findings that vary from subclinical alterations to alterations that influence prognosis and symptoms. Based on a more accurate diagnosis of endoprosthesis dysfunction, through the combined findings of echocardiography and tomography, we can identify the precise mechanism of dysfunction in post-TAVI follow-up, allowing for more adequate quantification of leaflet involvement and motion restriction and earlier onset of specific therapy.[14]

Author Contributions

Conception and design of the research: Costa A, Gomes LC, Junqueira B; acquisition of data: Junqueira B, Drubi S;

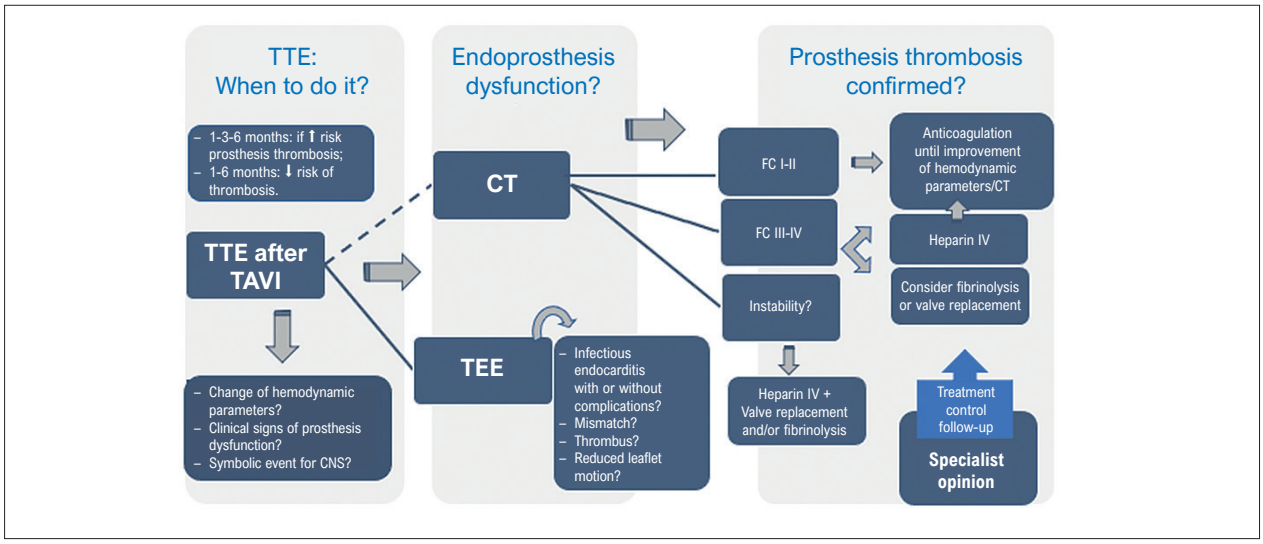

Figura 7 – *Algorithm for diagnosis and follow-up of prosthesis thrombosis after TAVI. TTE: Transthoracic echocardiography; CNS: central nervous system; TEE: transesophageal echocardiography; CT: computed tomography; FC: functional class according to NYHA; TAVI: transcatheter aortic valve implantation; IV: intravenous.*

writing of the manuscript: Gomes LC, Costa A, Drubi S; critical revision of the manuscript for intellectual content: de Melo RV, Guedes MB.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

This study is not associated with any thesis or dissertation work.

Ethics Approval and Consent to Participate

The study with the ethical aspects set forth in the Declaration of Helsinki of 1975. As this is a review study, in which clinical data, exams and therapeutic procedures, already performed in the routine of the service due to clinical indication, were used, we request the waiver of the free and informed consent form.

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