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REVIEW PAPER

Searching the perfect ultrasonic classification in assessing carotid artery stenosis: comparison and remarks upon the existing ultrasound criteria

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Abstract Doppler ultrasound scanning is the first line investigation for quantifying the internal carotid artery stenosis. Nevertheless, the lack of internationally accepted ultrasound criteria for describing the degree of stenosis has contributed to the different and confusing measurements ranges. The use of two different angiographic methods, the North American Symptomatic Carotid Endoarterectomy Study and the European Carotid Surgery Trial was probably the major initial source of confusion in deriving valid and reliable duplex ultrasound criteria worldwide. The consensus proposed in 2003 by the Society of Radiologists in Ultrasound has been a great attempt to create a conformity document, establishing grey scale and Doppler criteria in considering the different degrees of stenosis. According to this attempt, in 2010, the multi-parametric Deutsche Gesellschaft für Ultraschall in der Medizin ultrasound criteria have been proposed with a precise differentiation between main and additional criteria and depicted a different peak systolic velocity (PSV) threshold. In 2012, these criteria have been implemented, focusing on the multi-parametric approach, re-defining the PSV values and clearly introducing the concept of PSV average. Despite these attempts, a wide range of practice patterns still exists, with consistent disparities in patients' care. This paper collects these previous experiences and summarizes their strengths and weaknesses, to give a contribution in the carotid artery stenosis grading standardization using ultrasonic methods. Carotid ultrasound as the only diagnostic tool for the selection of patients for carotid surgery or stenting will be possible only with internationally accepted criteria.

Keywords Carotid artery stenosis · Ultrasound criteria · Standardization

Abstract L'eco-color Doppler dei tronchi sovra-aortici rappresenta la metodica non invasiva d'eccellenza per quantificare le stenosi carotidee. Tuttavia, la mancanza di criteri ultrasonografici di quantificazione del grado di stenosi universalmente accettati genera dati confondenti, spesso non equiparabili, con conseguente disparità di diagnosi, trattamento e costi. L'origine del dibattito ha avuto verosimilmente inizio a seguito della pubblicazione dei due maggiori trials angiografici, l'americano (NASCET) e l'europeo che definivano la quantificazione percentuale della stenosi dell' arteria carotide interna in maniera oggettivamente differente. Il documento di consenso del 2003 della Society of Radiologists in Ultrasound è stato il primo tentativo di standardizzazione dei criteri, prendendo posizione sui valori soglia di velocità del picco sistolico nella quantificazione della stenosi e considerando come riferimento il metodo NASCET. Nel 2010, la Società Tedesca di Ultrasonologia (Deutsche Gesellschaft für Ultraschall in der Medizin, DEGUM), ha proposto un approccio di quantificazione multi-parametrico con percentuali di graduazione più definite e con differenti valori soglia di velocità rispetto alla proposta precedente prendendo in considerazione valori di velocità di picco sistolico (PSV) di 200 cm/s rispetto a PSV di 125 cm/s per stenosi NASCET del 50 %. Un' ulteriore

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nuova proposta classificativa, comparsa sulla rivista *Stroke* nel 2012, non pare a tutt'oggi aver risolto del tutto il problema. La presenza di fatto di 2 valori soglia di PSV nettamente diversi, ha amplificato drammaticamente la disparità nella quantificazione della percentuale di stenosi. Permangono quindi evidenti discrepanze nella refertazione e nella comparabilità dei dati tra i diversi centri. Gli Autori hanno dunque tentato una rivisitazione critica delle classificazioni in uso e proposto un ulteriore contributo, nell'attesa di linee guida universalmente accettate che consentano una maggiore uniformità diagnostica.

Introduction

Duplex sonography is nowadays the first line of investigation to detect and classify the carotid artery stenosis severity.

This technique was first pioneered and then developed in 1970s at the University of Washington by Dr. D. E. Strandness Jr, a vascular surgeon, who greatly implemented the field of vascular ultrasound.

His laboratory established criteria for interpretation of all duplex scanning, including carotid disease, based on the Doppler information and on the B-mode images of the vessels.

The parameters used to classify the severity of the carotid disease included peak systolic velocity (PSV), the spectral broadening degree, the end diastolic velocity and the overall waveform shape. These features allowed to create a carotid bifurcation stenosis classification, the so-called "Strandness criteria" [1].

These criteria were developed to predict the carotid bulb diameter reduction, using six stenosis severity categories (none, 1–15, 16–49, 50–79, 80–99 % diameter reduction and complete occlusion) [1], with high sensitivity and specificity when compared with angiography.

Then, in the 1990s, the large trials in symptomatic and asymptomatic patients, as explained in the dedicated paragraph, contributed to the growing debate in the classification criteria, with the rise of criticism about the previous ones.

Nevertheless, the lack of internationally accepted ultrasound criteria for describing the degree of stenosis is nowadays a topical question.

This paper collects these previous experiences and summarizes their strengths and weaknesses, to give a contribution in the carotid artery stenosis grading standardization using ultrasonic methods.

The structure of this paper allows the reader to be guided in the critical examination of the historical studies and of the "post Strandness" classifications, with the aim of making him able to be harshly critic or in accordance with the final Authors' classification proposal.

The origin of the grading debate: the large trials in symptomatic and asymptomatic patients

The use of two different methods to calculate the degree of stenosis was probably the major initial source of confusion in deriving valid and reliable duplex ultrasound criteria worldwide.

The studies of carotid artery disease have historically classified the patients in two groups: the symptomatic (patients who experienced a stroke, a transient ischemic attack or fugax amaurosis due to cerebral ischemia), and the asymptomatic ones (without a neurological event but only clinical marks of atherosclerosis).

The North American Symptomatic Carotid Endarterectomy Trial (NASCET) [2], the European Carotid Surgery Trial (ECST) [3, 4] and the Asymptomatic Carotid Artery Study (ACAS) [5] have been the major trials for the symptomatic and the asymptomatic patients, respectively.

According to the NASCET method, the stenosed lumen is compared with the lumen of the distal internal carotid artery (ICA), so the degree of the stenosis is determined in relation to the distal lumen, while according to the ECST, the degree of the stenosis is determined in relation to the original lumen.

The ECST method results in higher degrees of stenosis and so the conversion to NASCET and vice versa has been established, according to the well-known conversion formula: NASCET % = (ECST-40) %/0.6 and ECST % = 40 + (0.6 × NASCET %) [6].

The initial results from the NASCET reported significant beneficial effect of carotid endarterectomy in patients with high degree carotid artery stenosis (70–99 %), while for patients with stenosis <70 %, the trial revealed modest benefit in selected patients (with degree of stenosis 50–69 %).

For asymptomatic patients, the ACAS showed a benefit when the stenosis was greater than 60 % [5].

The consensus of the society of radiologists in ultrasound (2003)

The consensus statement proposed in 2003 by the Society of Radiologists in Ultrasound [7] has been a great attempt to create a conformity document in assessing the carotid artery stenosis.

This consensus [7] exposed technical considerations, in particular about the recommended angulation (insonation angle less than or equal to 60°) and about the key components of the ICA examination.

The consensus panel established grey-scale and Doppler criteria that considered different degrees of stenosis. The well-known table (Table 3 in [7]), a reference for many

years, summarized the primary (ICA PSV, and plaque estimate in percentage) and the additional parameters (the ICA/common carotid artery, CCA, ratio and the ICA end diastolic velocity, EDV) for the diagnosis of ICA stenosis classifying the degree of stenosis (%) in six categories.

The panel recommended the use of the NASCET method.

As considered further in this paper, the consensus of the Society of Radiologists in Ultrasound has the strength to be rather simple and immediate, with a clear definition of the concept of the "near occlusion", besides having precisely defined the role of the NASCET method as of choice in assessing the ICA degree of stenosis.

The degum revision (2010)

The German Society ultrasound criteria for assessing the ICA stenosis [8] were exposed in 1986, following the ECST method, but, to overcome the confusion caused by the coexisting NASCET, in 2010 the Deutsche Gesellschaft für Ultraschall in der Medizin (DEGUM) proposed a multi-parametric approach, consisting of combined Doppler and imaging criteria, referring at this time to the NASCET definition [9] and considering, obviously, the classification of Radiologists [7].

The multipara-metric DEGUM ultrasound criteria, as summarized in the well-known table (Table 1 in [9]) allows a grading of severe stenosis in steps of 10 %, so it is possible to differentiate between a stenosis of 70, 80, 90 % or occlusion. Moreover, the importance of the post-stenotic PSV was underlined.

A different PSV threshold was proposed, considering the value of 200 cm/s for 50 % ICA stenosis according to the NASCET method, instead of >125 cm/s, as mentioned by the Society of Radiologists in Ultrasound. This point is crucial: it has generated new insight and subsequent consequences in the stenosis quantification.

The NASCET method has been primarily considered, but also the ECST maintained its validity.

Otherwise, the classification appears more entangled to understand and the concept of the near occlusion is less clear.

The neurosonology research group of the world federation of neurology multiparametric criteria (The *Stroke* 2012 summarizing report on behalf of)

The continuous lack of internationally accepted ultrasound criteria for describing the degree of stenosis has led to a further attempt to improve the previous classification criteria, so a dedicated paper appeared in 2012, published in *Stroke* journal [10] with the aim to summarize the worldwide available experiences after the consensus proposed in 2010.

The difficulty to create a general statement about the reliability of the Doppler ultrasound rises from the fact that there are not universally accepted criteria and no consensus about the relative weight of each parameter. However, the multi-parametric approach, in our opinion, remains the best choice that has to be implemented. As explained in [10], the main criteria represent the essential morphologic and hemodynamic information, while the secondary or additional criteria represent supporting elements, generally more difficult to quantify. In particular, the consensus has considered as *main criteria* the B-mode and colour imaging, the mean or threshold values of PSV, the post-stenotic velocity and the appearance of collateral flow (ophthalmic artery, Willis' circle), while as *secondary criteria* the pre-stenotic reduced flow in the CCA, the post-stenotic disturbances, the end diastolic flow velocity in the stenosis and the carotid ratio (ICA/CCA velocities).

This paper has greatly supported the concept that PSV alone was a too much simplified diagnostic parameter and then not sufficient. In fact, the increased velocities in stenosis fall to happen in situations of near occlusion, moreover the presence/absence of collateral flows may affect the PSV values.

This is the summarized main steps of the grading classification:

- 0–40 % NASCET low degree of stenosis: evaluation in B-mode imaging, in longitudinal and cross-sectional planes, adding information about the percentage of diameter reduction, the thickness and length of the plaque and the residual lumen;
- 50–60 % NASCET moderate degree of stenosis: local increase of velocity (PSV <230 cm/s) without collateral flows (this point creates a further differentiation from 2003 and 2010 in terms of the PSV threshold);
- ≥70 % NASCET relevant degree of stenosis: combined evaluation of the hemodynamic criteria (PSV >230 cm/s, presence of collateral flows, increased end diastolic velocity). Moreover the evaluation of the degree of the reduction of post-stenotic flow allows to differentiate between 70, 80 and 90 % stenosis.

In this classification (as reported in Table 3 in [10]) despite an apparent structure similarity with the DEGUM, it is remarkable that there is a sort of up-turn to the PSV value proposed in 2003 for the 50 % stenosis (PSV threshold 125 cm/s), but the Authors underline that it is a too simplified parameter. To overcome the possible scat-

tering of results, they suggest to quantify and clearly report also the PSV average (cm/s) that, in combination with the other criteria, could discriminate whether the measured PSV is to be considered a less or more severe stenosis within the scatter range.

It is affirmed that in case of clear reduction of PSV (<30 cm/s), the estimate of diameter reduction is about 90 % and the residual lumen is <1 mm.

There is also the recommendation to use the lowest possible angle of insonation, but without the precise limits (this point will be widely discussed forward).

The real worldwide outcomes to the problem

In current clinical practice, the lack of an universally accepted and validated consensus authorizes the clinicians to adopt a number of different values for velocities and derived indexes and this source of variation and the confusion in the diagnostic criteria explain some disparities in care.

A recent paper [11] systematically analysed the institutional differences in carotid artery duplex criteria in some United States of America centres and these different criteria resulted in a significant variation in the classification of the stenosis that led to consistent differences in clinical decision making, and in the number of revascularizations. In fact, Authors demonstrated a great variability in the number of carotid revascularization, and finally in health costs, comparing 10 institutions.

The practice to create standardized approaches fitted to individual centres or working groups [12, 13] confirms this variability and the need of worldwide accepted criteria. The monitoring of patients participating even in carotid artery therapy clinical trials at the University of Washington has shown [12] disparities and disagreement about how the examination should be performed and how the results should be validated. Authors proposed an unifying ultrasound reading centre to analyse the measurements, with the evidence of worldwide attempts to standardize the technique.

A similar effort has been presented in United Kingdom [13] with a dedicated working group for acquiring, interpreting and reporting carotid ultrasound investigations as homogenously as possible.

It is clearly evident that the complexity of the problem and the different used criteria (not always declared) with subsequent practice dissimilarities in the report not only between different specialists (Radiologist, Neurologists, Internists and Vascular Surgeons), or scientific societies, but even inside each institution.

Comments, comparison and remarks between the previous criteria

Despite its immediacy and easy interpretation, the consensus of the Society of Radiologists in Ultrasound [7] appears to be too simplified. In fact, the subsequent multiparametric approaches offer the possibility of using both morphological and hemodynamic criteria. Moreover, the multi-parametric approaches [9, 10] allow a stenosis grading in steps of 10 %, that could not be possible using the Radiologists' classification [7].

The PSV results only of limited value if considered alone, because of the well-known factors that influence it: the Doppler angle, the spectrum analysis, the morphology of the stenosis, the collaterals and the particular situation of the nearly occluded artery, as recently reviewed [14].

All the correlations between PSV and angiography showed a considerable scatter due to the fact that the diameter reduction is measured by angiography but the hemodynamic effect of a stenosis is due to the area reduction degree, so it is obvious that discrepancies between the two different techniques (ultrasonic and angiographic) exist. That is why additional criteria are mandatory.

This is also the background of the introduction of the evaluation of the PSV average [9, 10], that could also be considered as a threshold value.

Moreover, PSV is insufficient to differentiate between severe and very severe stenosis (so between 70 and 80–90 % stenosis): the post-stenotic flow velocity in the segment distal to the disturbed flow is the criterion that helps this discrimination, as well explained in [10] (it has to be noticed that in this area the Radiologists' consensus was lacking in terms of precise velocity values, despite a clear consideration of the concept of near occlusion).

Table 1 summarizes the main characteristics of the previous criteria for grading the ICA stenosis.

The authors' proposal for grading the ICA stenosis: the Doppler criteria

Table 2 summarizes the Doppler criteria for grading the ICA stenosis, according to the Authors'proposal. There are evident similarities both with the DEGUM criteria and with the Neurosonology Research Group criteria, obviously. Authors have appreciated the multi-parametric approach, the narrow grading percentage of the ICA stenosis of both the classification criteria, with particular consideration to the DEGUM with respect to the double NASCET/ECST classification with the different PSV threshold proposed,

Table 1 The comparison of the main characteristics of the previous criteria for grading the internal carotid artery stenosis

Main characteristics	The consensus of the society of radiologists in ultrasound (2003)	The degum revision (2010)	The Neurosonology Research Group criteria (2012)
Easy to interpret and immediate	+++	+	+
Multi-parametric approach	+	++	+++
NASCET + ECST method	Only NASCET	+++	Only NASCET
% Detailed ICA degree of stenosis (grading in multiple steps)	+	+++	+++
Congruence of PSV values with angiogram curves and clinical menagement	+	+++	+++
Post-stenotic PSV evaluation	–	+++	+++
Clear concept of "near occlusion"	+++	–	–
Concept of "PSV average"	–	+	++
Insonation angle (very precise indications about)	–	–	–

DEGUM Deutsche Gesellschaft für Ultraschall in der Medizin, *NASCET* North American Symptomatic Carotid Endoarterectomy Study, *ECST* European Carotid Surgery Trial, *ICA* internal carotid artery, *PSV* peak systolic velocity; + only in part considered and explained; ++: considered and explained; +++: considered and explained with particular attention; –: not mentioned nor substantially considered

Table 2 The Doppler criteria for grading the internal carotid stenosis according to the Authors' proposal

Degree of stenosis (NASCET) (%)	10	20–40	50	60	70	80	90	Occlusion
Degree of stenosis (ECST) (%)	40	50–60	70	75	80	90	95	Occlusion
Intra-stenotic PSV threshold (cm/s)		115–160	200	250	300	350–400	100–500	
Intra-stenotic end diastolic flow velocity (cm/s)				100	100	>100	>100	
Post-stenotic PSV (cm/s)					>50	<50	<30	
Carotid ratio (ICA/CCA)				≥2	≥2	≥4	≥4	
Pre-stenotic diastolic flow (cm/s)					Possibly reduced	Reduced	Reduced	Reduced

NASCET North American Symptomatic Carotid Endoarterectomy Study, *ECST* European Carotid Surgery Trial, *PSV* peak systolic velocity, *ICA* internal carotid artery, *CCA* common carotid artery

considering the value of 200 cm/s for 50 % ICA stenosis according to the NASCET, that appears not to create the misunderstanding (at 50 and 70 %) that could be possible in the *Stroke* classification, where the concept of PSV average could induce the physician to be uncertain about the true value, in the absence of the quantification of all criteria.

Authors recommend to consider the PSV threshold of 200 cm/s in case of asymptomatic patients, instead of PSV threshold of 160 cm/s in case of symptomatic ones, leading to better address patients to carotid endartherectomy. In particular, the PSV threshold of 200 cm/s allows to discriminate between asymptomatic patients who have increased or decreased risk for ipsilateral stroke or harms after carotid endarterectomy or carotid angioplasty and stenting, avoiding possible prevention excesses, as reviewed in a recent paper [15]: the aim was to evaluate the current evidence on whether screening asymptomatic adults for carotid artery stenosis reduced the risk for ipsilateral stroke, showing that not invasive screening with ultrasonography resulted in many false-positive results. On the other hand, in symptomatic patients' evaluation, the findings of PSV >160 cm/s but <200 cm/s, must alert the operator to suspect a 50 % NASCET stenosis. So, the patient's condition, the evaluation of the plaque characteristics and the additional parameters allow to be more flexible and "patient's orienteered". Nevertheless, during the last decades, after the wide acceptance of the NASCET results, Doppler ultrasound has proceeded to fit threshold values to various sets of data to optimize agreement with "NASCET-style" angiographic measurements, rather than developing new ultrasound parameters more consistent with the NASCET methodology, so a scatter of results will be almost unavoidable.

The authors' proposal for grading the ica stenosis: the final "ten commands" for the colour Doppler sonographer

In the Authors' proposal, the evaluation of the ICA stenosis should be completed with the following information:

1. the plaque location;
2. the plaque extension and the plaque maximal diameter (mm), trasversal and/or longitudinal section;
3. the plaque surface details (smooth, irregular, very irregular);
4. the Gray-Weale echogenicity classification [16, 17] report: type 1: uniformly anechoic or hypoechoic; type 2: predominantly (>50 %) hypoechoic; type 3: predominantly (>50 %) hyperechoic; type 4: uniformly hyperechoic and type 5: uniformly echogenic with posterior shadowing (the so called calcified plaque);
5. the report of the area or diameter reduction (according to both the NASCET method and the ECST) with the clear declaration of the % of stenosis according to the NASCET method and, in brackets, to the ECST;
6. the intra-stenotic PSV and end diastolic flow velocity (cm/s), the pre- and post-stenotic PSV (cm/s) evaluation;
7. the carotid PSV ratio ICA/ACC;
8. the evaluation of the collateral flows;
9. the Doppler insonation angle;
10. the Trans-Cranial Colour Doppler (TCCD) evaluation.

Some remarks about some points: first of all, it seems reasonable the report of both ECST and NASCET stenosis percentage, as considered in the DEGUM classification, because of the effective difference of the percentage of the diameter reduction (local diameter reduction according to the ECST and distal diameter reduction according to the NASCET). The diameter related to the distal diameter better corresponds to the hemodynamic effects but the local diameter narrowing better shows the plaque burdening. The NASCET classification is not correctly applicable in the cases of a severe stenosis, in which there is a decrease of the post-stenotic flow volume that leads to a lower calculated stenosis degree. So, it can be affirmed that as the stenosis becomes more severe, as the hemodynamic criteria should prevail. In eccentric plaques, the diameter and the area reduction are similar, but in concentric ones, the stenosis degree, measured in percentage reduction, is higher than the measured diameter reduction. That is why Authors consider that both methods should be declared.

As reported [7], the consensus of the Society of Radiologists in Ultrasound recommended that the Doppler waveform should be obtained with an insonation angle "less than or equal to 60°", while the Neurosonology Research Group criteria [10] stated that measurements should be taken using the angle "as lowest as possible".

Going on, in the Authors' opinion, the insonation angle has to be considered as correct if equal or less than 45°, not than 60°, as previously recommended. This is an intriguing point.

So, it is clear that the possible error is greater as greater is the angle, due to its cosine function in the Doppler equation. The angle can be estimated reasonably well in laminar flow conditions, but this is not always possible in disturbed or turbulent flows. Any error in setting the Doppler angle significantly increases errors in velocity measurements and the final result of an incorrect insonation angle is that the measured PSV increases. Nowadays, it is not tolerable accepting an insonation angle of 60° as correct because of the percentage of PSV increase and because of the subsequent change in the carotid stenosis percentage classification. It is to mention, however, that in some conditions a low angle is very difficult to acquire, so it is not realistic recommending an insonation angle equal or less than 30°. In fact, few examinations could be performed with this angle, that is surely the best, but it is applicable only in selected patients: so this value has to be the goal, the objective but, in Authors' opinion, should not be the daily rule.

Authors care to remark the contribution of the TCCD evaluation in the context of carotid ultrasound. Collateral flow evaluation (in particular periorbital arteries or Willis' circle) has been established [10] as additional criteria. The evaluation of the ophthalmic artery, that is the most important collateral artery between the external and internal carotid arteries, is possible using the standard Doppler ultrasound, but the collaterals of the anterior communicating and posterior communicating arteries require the TCCD. In severe stenosis or occlusion there is a clear sonographic evidence of collaterals. Authors suggest the TCCD evaluation in patients with ICA stenosis $\geq$70 % as integrative information. In fact, the hemodynamically compromising ICA lesion can reduce the downstream velocities in the middle cerebral artery (MCA) without its own or ICA disease, so an upstream ICA obstruction has to be ruled out to ascribe an intracranial flow reduction to intracranial pathology. Infact, a significative PSV reduction in MCA could underline the importance of the stenosis in the ipsilateral ICA.

It has been well established that the TCCD should be considered to evaluate the risk of stroke recurrence with particular attention to the characteristics of the MCA (the

recommendation of the TCCD in the context of *acute* stroke has been well established, as exposed in [18]).

Nevertheless, increasing evidence suggests that also asymptomatic intracranial arteries stenosis is associated with traditional cardiovascular risk factors and that this finding is an independent predictor of vascular mortality [19–23] so the importance of screening asymptomatic intracranial stenosis has not to be omitted, according to these recent studies (no definitive results has been reached in this area, that is why more attention has to be paid to this point).

Conclusions

The exact grading of the ICA stenosis is the crucial step in the optimal patient management. This paper has tried to give a contribution in the area of the ultrasound classification of the ICA stenosis, collecting previous experiences and summarizing their strengths and weaknesses but it is also the result of the comparison of these previous existing criteria linked with the Authors' experiences.

The lack of worldwide uniformity in the interpretation criteria and in the different laboratories reports makes this work difficult, nevertheless, carotid ultrasound as the only diagnostic tool for the selection of patients for carotid surgery or stenting will be possible only with internationally accepted criteria.

This goal will be the first step for assessing the whole imaging-based risk stratification strategies that have to take into account factors beyond the luminal stenosis measurements, including cerebral hemodynamics and plaque composition, data achievable with advanced imaging techniques in order to create a multifactorial risk assessment strategy as recently considered [24].

This work presents several limitations: no data and comments are provided about the Doppler ultrasound criteria for the stented carotid artery, no comments are given about the necessity or not for further arterial evaluation in severe carotid stenosis found on ultrasound (computed tomography angiography, magnetic resonance angiography).

Authors' aim has been giving only a little contribution in this area, considering the standardization a precise goal for the carotid arterial stenosis, with the consciousness that the debate remains still open.

Compliance with ethical standards

Conflict of interest Authors declare that they have no conflict of interest.

Informed consent All procedures that have permitted Authors to write this review were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000. All patients involved provided written informed consent to enrolment in the study and to the inclusion in this article of information that could potentially lead to their identification.

Human studies The studies that have conducted Authors to write this review article were conducted in accordance with all institutional and national guidelines for the human studies.

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