CLINICAL SCIENCE

The provisional OMERACT ultrasonography score for giant cell arteritis

Christian Dejaco,[1,2] Cristina Ponte,[3,4] Sara Monti,[5,6] Davide Rozza,[7] Carlo Alberto Scirè,[8] Lene Terslev,[9,10] George A W Bruyn,[11] Dennis Boumans,[12] Wolfgang Hartung,[13] Alojzija Hočevar,[14,15] Marcin Milchert,[16] Uffe Møller Døhn,[17] Chetan B Mukhtyar,[18] Markus Aschwanden,[19] Philipp Bosch,[1] Dario Camellino,[20] Stavros Chrysidis,[21] Giovanni Ciancio,[22] Maria Antonietta D'Agostino,[23,24] Thomas Daikeler,[25] Bhaskar Dasgupta,[26] Eugenio De Miguel,[27] Andreas P Diamantopoulos,[28] Christina Duftner,[29] Ana Agueda,[30] Ulrich Fredberg,[31,32] Petra Hanova,[33,34] Ib Tønder Hansen,[35] Ellen-Margrethe Hauge,[36,37] Annamaria Iagnocco,[38] Nevsun Inanc,[39] Aaron Juche,[40] Rositsa Karalilova,[41] Toshio Kawamoto,[42,43] Kresten Krarup Keller,[36,44] Helen Isobel Keen,[45] Tanaz A Kermani,[46] Minna J. Kohler,[47] Matthew Koster,[47] Raashid Ahmed Luqmani,[48] Pierluigi Macchioni,[49] Sarah Louise Mackie,[50] Esperanza Naredo,[51] Berit Dalsgaard Nielsen,[36,52] Michihiro Ogasawara,[43] Carlos Pineda,[53] Valentin Sebastian Schäfer,[54] Luca Seitz,[55] Alessandro Tomelleri,[56] Karina D Torralba,[57] Kornelis S M van der Geest,[58] Kenneth J Warrington,[47] Wolfgang A Schmidt[59]

膠原病・リウマチ内科　ジャーナルクラブ

2023年1月24日

岡 秀樹

背景

- エコーでは, 均一でhypoechoicな血管壁肥厚を認め, “halo sign”と呼ばれている.
- 治療後に側頭動脈(TA)のintima-media thickness(IMT)は急速に減少, 腋窩動脈(AX)は緩徐に減少.
- 治療で, 内膜はhypoechoic→isoechoic/hyperechoicな変化をする(multilinear pattern).
- GCA 45名の6カ月,12カ月,24カ月後のエコーのフォローでは, TAの85%で内膜の減少を認めた.
- GUSTO試験では, パルス後にIMT減少するが,TCZ単独では増加し, その後徐々に低下.
- 薬剤がCRP/ESRに影響を及ぼすため, 疾患活動性や治療効果判定の指標が必要であった.
- Outcome Measures in Rheumatology (OMERACT) ultrasonography large vessel vasculitis working groupが, GCA超音波スコアを作成した.

Vasculitis

CLINICAL SCIENCE

Ultrasound halo sign as a potential monitoring tool for patients with giant cell arteritis: a prospective analysis

Cristina Ponte,[1,2] Sara Monti,[3,4] Carlo Alberto Scirè,[5,6] Paolo Delvino,[3] Nikita Khmelinskii,[1,2] Alessandra Milanesi,[3] Vitor Teixeira,[1,7] Fabio Brandolino,[3] Fernando Saraiva,[1] Carlomaurizio Montecucco,[3] João Eurico Fonseca,[1,2] Wolfgang A Schmidt,[8] Raashid Ahmed Luqmani[9]

Halo singは治療経過と共に改善していく.
腋窩動脈の改善は側頭動脈と比べて緩徐.

Ann Rheum Dis. 2021;80(11):1475-1482.

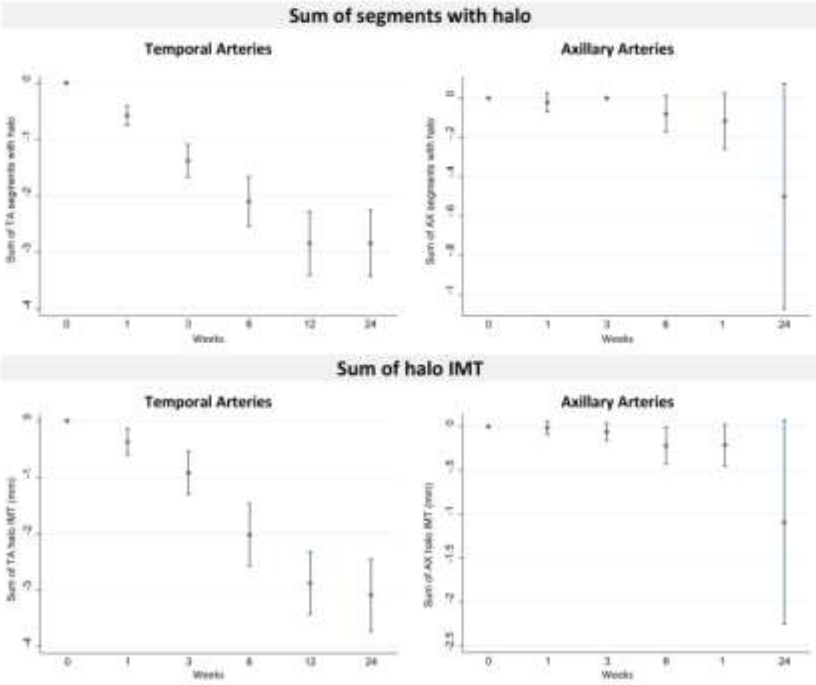
GCAでのHalo signを前向きにモニタリングして有用性を検討した初の研究(欧州,PROTEA study).

新規発症, PSL<15mg/日, TA/AXにHalo singを認めるGCA49名で, 0,1,3,6,12,24wに臨床/検査/超音波データが評価された.
寛解は,PSL<30mg/日で再発がないことと定義.
超音波：８領域のHalo singとIMTを測定. IMTは径が最大径になる所で縦断で測定.

超音波検査の前に高容量PSLを平均 2.5日間投与されていた.
24.5%にパルスが既に行われていた.

- Halo sign

Baseline TA:47/49(97%), AX:11/49(22%), TA+AX:9/49(18%)
時間経過と共にHalo singのセグメントとIMTは減少する.
AXに関してはTAよりも改善が緩徐



TAはHaloセグメント数とIMTの厚さが疾患活動性と相関するがAXはしない.
PSL累積投与量は負の相関.
AXは相関しない.

Table 4 Association between halo features and disease activity markers

	Correlation coefficient			OR
	ESR*	CRP*	BVAS	Disease remission
Number of arterial segments				
Sum of all segments with halo	0.44	0.36	0.29	0.47
Sum of TA segments with halo	0.41	0.34	0.29	0.39
Sum of AX segments with halo	0.08	0.06	0.04	1.41
Halo thickness				
Sum of all halo IMT (mm)	0.47	0.40	0.34	0.51
Sum of TA halo IMT (mm)	0.44	0.39	0.36	0.34
Sum of AX halo IMT (mm)	0.09	0.07	0.06	1.41
Maximum TA halo IMT (mm)	0.48	0.41	0.35	0.34
Maximum AX halo IMT (mm)	0.08	0.07	0.04	1.38


Imaging

CLINICAL SCIENCE

Novel ultrasonographic Halo Score for giant cell arteritis: assessment of diagnostic accuracy and association with ocular ischaemia

Kornelis S M van der Geest,[1,2] Frances Borg,[3] Abdul Kayani,[3] Davy Paap,[1,3] Prisca Gondo,[3] Wolfgang Schmidt,[4] Raashid Ahmed Luqmani,[5] Bhaskar Dasgupta[3]

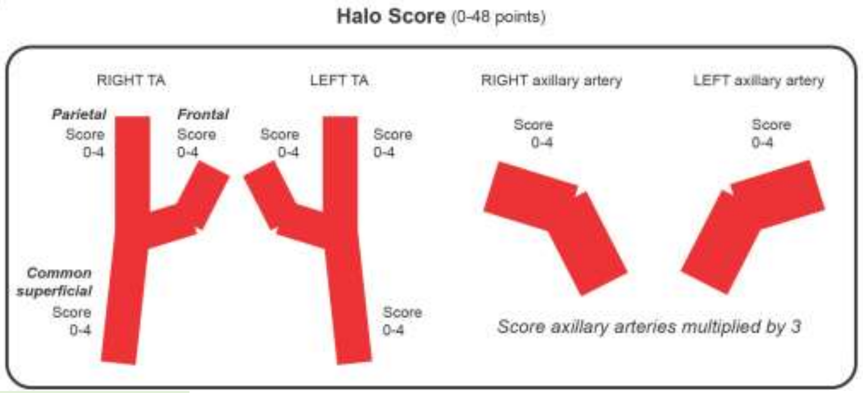
Halo scoreとHalo countを提唱した研究.

Ann Rheum Dis. 2020;79(3):393-399.

Halo Grading	Common superficial TA halo thickness (mm)	Parietal TA halo thickness (mm)	Frontal TA halo thickness (mm)	Axillary artery halo thickness (mm)
Grade 0	0.3 or less	0.2 or less	0.1 or less	0.5 or less
Grade 1	0.4	0.3	0.2	0.6
Grade 2	0.5	0.4	0.3	0.7-0.8
Grade 3	0.6-0.7	0.5*	0.4	0.9-1.5
Grade 4	0.8 or more	0.6 or more	0.5 or more	1.6 or more

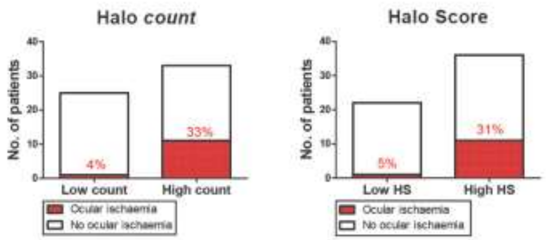
GCA疑いの89名の内, 超音波とTABで58名のGCAが確定.
超音波とTABはPSL投与7日以内に行われた.
Halo signの定義:血管内腔に暗い低エコー域

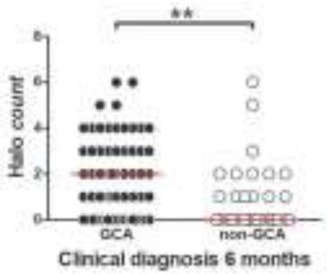
D

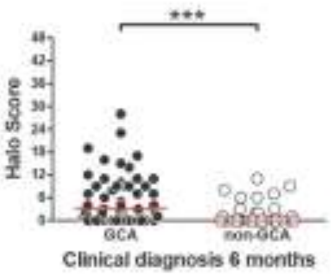


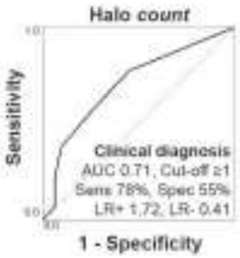
浅側頭動脈本幹と頭頂枝,前頭枝,腋窩動脈のIMTからscoreを作成.
腋窩動脈と側頭動脈を同じ重みづけにするために3倍とした.合計48点.
Halo countは8点満点.

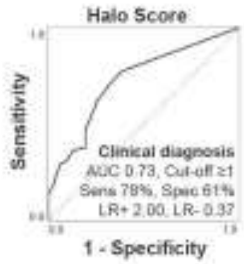
- GCAでHalo scoreとHalo countはnon-GCAより高値.
- Halo count≥1: 感度75%,特異度 55%,LR+ 1.72
- Halo score≥1: 感度78%,特異度61%,LR+2.0
- 特異度95%を示すには,Halo count≥6, Halo socre≥10.
- Halo socre≥10でLR+ 6.41, Halo countはLR+1.07
- TAB+はTAB-よりHalo score/count共に高値. LR>2でTABの結果予測に役立つ
- 眼球虚血:Halo score≥2 OR 9.88, Halo count≥3 OR12.00.
- Halo scoreはCRPと相関するが, TAのみのsub解析では否定的.

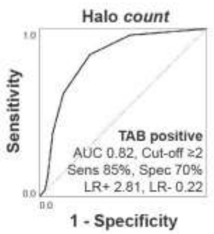


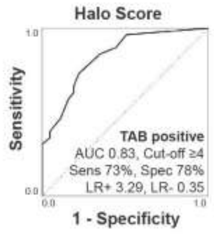


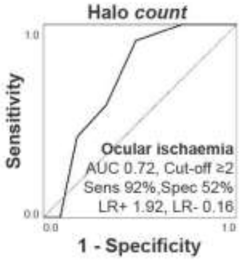


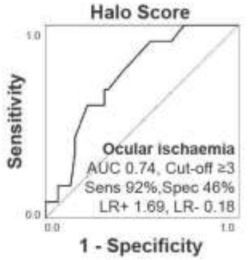













RHEUMATOLOGY

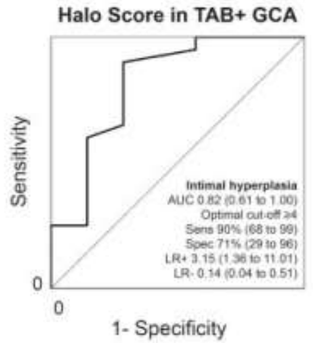
Concise report

Ultrasonographic Halo Score in giant cell arteritis: association with intimal hyperplasia and ischaemic sight loss

Kornelis S. M. van der Geest[1,2], Konrad Wolfe[3], Frances Borg[2], Alwin Sebastian[2], Abdul Kayani[2], Alessandro Tomelleri[2], Prisca Gondo[2], Wolfgang A. Schmidt[4], Raashid Luqmani[5] and Bhaskar Dasgupta[2]

Halo score高値は内膜過形成と眼球虚血と関連あり

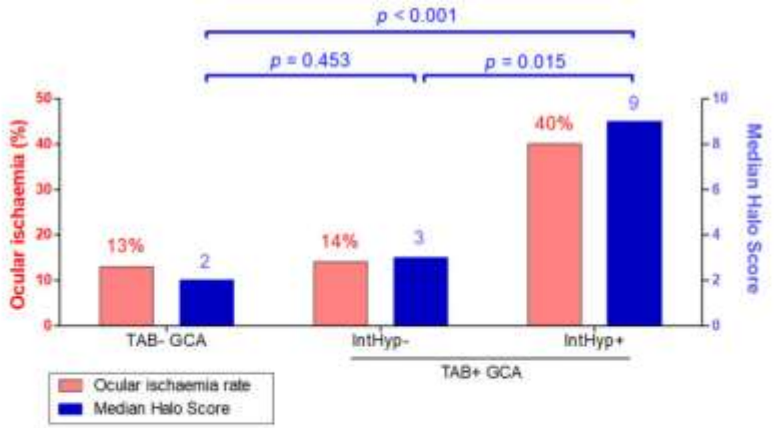
Rheumatology (Oxford). 2021:60(9):4361-4366.



Halo score高値とTABの内膜過形成,眼球虚血の関係を検証(TABLE studyのsub解析).

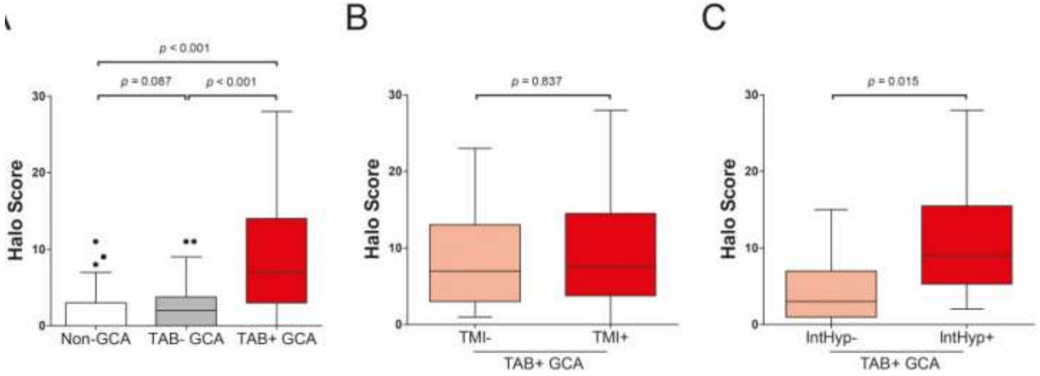
[背景] Halo sing=intima-media complexの厚さ.
Halo score高値=内膜過形成と関連を予想.
Halo score高値と眼球虚血は関連.
内膜過形成と眼球虚血は関連

GCAが疑われる92名
超音波ではPSL開始7日以内, 8領域のIMTを評価.
TABはPSL開始後14日以内に行われた.
病理所見では, 血管壁を超える炎症細胞の浸潤, 巨細胞, 内膜過形成が評価.



TAB+GCAは27人(33%に眼球虚血あり)
TAB-GCAは32人(13%に眼球虚血あり)
それ以外31人はnon-GCA(23%に非動脈性の眼球虚血あり)
内膜過形成は20/27で見られた.

血管壁を超える炎症性細胞の浸潤はHalo scoreと関連せず.
巨細胞はほぼ全てのTABで検出されていたため比較できず.
内膜過形成はHalo score高値と関連あり(多変量解析 p=0.001).
Halo score≥4で感度90%,特異度70%,LR+3.15
内膜過形成があり, Halo score高値は眼球虚血と関連



Vasculitis

ORIGINAL ARTICLE

RMD Open
Rheumatic & Musculoskeletal Diseases

Definitions and reliability assessment of elementary ultrasound lesions in giant cell arteritis: a study from the OMERACT Large Vessel Vasculitis Ultrasound Working Group

Halo sign, Compression singの定義

RMD Open. 2018;4(1):e000598.

①GCAの超音波所見をsystematic literature review
②Delphi法で超音波所見のコンセンサスを作成
③実際に手技者間と手技者内での信頼性を評価

SLRを行った後,25のstatementを作成して, GCAの経験が豊富な25名の医師にメールを送った.
信頼性の評価では,TA/AXの正常を含む静止画・動画で行われた.

Halo sign: 均一な低エコーの壁肥厚で, 内腔側に向かうとよく描出され, 横断面で最も同心円状に描出される.
Compression sign:圧迫すると肥厚した血管壁が見える. 低エコーの血管壁肥厚は,中~高エコーの周囲組織と対照的.

評価者間,評価者内では, 横断・縦断の静止画・動画の κ >0.8で信頼性は良好であった.

Domain	Definition	Agreement (%)	Delphi round
US appearance of			
normal temporal arteries	Pulsating, compressible artery with anechoic lumen surrounded by mid-echoic to hyperechoic* tissue. Using US equipment with high resolution, the intima-media complex presenting as a homogenous, hypoechoic or anechoic echostructure delineated by two parallel hyperechoic margins ('double line pattern') may be visible.	95.7	1
normal extracranial large arteries	Pulsating, hardly compressible artery with anechoic lumen; the intima-media complex presents as a homogenous, hypoechoic or anechoic echostructure delineated by two parallel hyperechoic margins ('double line pattern'), which is surrounded by mid-echoic to hyperechoic tissue.	100	1
arteriosclerotic arteries	Heterogeneous and in part hyperechoic, irregularly delineated and eccentric vessel wall alteration.	95.8	2
'halo' sign	Homogenous, hypoechoic wall thickening, well delineated towards the luminal side, visible both in longitudinal and transverse planes, most commonly concentric in transverse scans.	91.3	2
stenosis in temporal arteries	A stenosis is characterised by aliasing and persistent diastolic flow by colour Doppler US. The maximum systolic flow velocity determined within the stenosis by pulsed wave-Doppler US is ≥2 times higher than the flow velocity proximal or distal to the stenosis.	95.8 100	2 3
stenosis in extracranial large arteries	Typical vasculitic vessel wall thickening with characteristic Doppler curves showing turbulence and increased systolic and diastolic blood flow velocities.	75	1
occlusion	Absence of colour Doppler signals in a visible artery filled with hypoechoic material, even with low pulse repetition frequency and high colour gain.	87.5	1
'compression' sign of temporal arteries	The thickened arterial wall remains visible upon compression; the hypoechogenic vasculitic vessel wall thickening contrasts with the mid-echogenic to hyperechogenic surrounding tissue.	78.3	1
US assessment of			
'compression' sign of temporal arteries	The compression sign should be assessed by applying pressure via the transducer until the lumen of the temporal artery occludes and no arterial pulsation remains visible.	91.3	1

方法

- **Step 1(先行研究)**

過去のGCAの超音波所見の文献をreview
急性・慢性GCAの超音波所見の合意,
その所見が経験豊富な超音波技師が行いGCA診断の信頼性を評価

- **Step 2**

GCA超音波スコアについてのコンセンサスをDelphi法で実施

- **Step 3**

信頼性の評価

- **Step 4**

最終合意と心理特性の評価

Step 2

- Delphi法を7ラウンド行った.

38個の質問が準備された.

超音波検査の経験に関すること, 仕事や環境の影響, どの動脈を含めるか, どこでどのようにIMTを測定するかなど.

回答には5段階のLikert scaleが用いられた(0:強く反対,,,,5:強く賛成).

75%が4 or 5の回答を得たstatementはコンセンサスが得られたとした.

それ以外はWGメンバーにて修正され次のラウンドに回された.

Supplementary File 1. Questionnaire for the first Delphi round for the development of an OMERACT GCA ultrasound score

Question	Question type
Q1. Statement: The score should include the right and left common superficial temporal arteries with their frontal and parietal branches (6 segments) and the axillary arteries (2 segments)	Rating 1-5
Q2. Statement: An additional extended OMERACT Ultrasound Score is recommended which includes the right and left facial, occipital, common carotid, subclavian and vertebral arteries in addition to the temporal and axillary arteries	Rating 1-5
Q3. Statement: In addition to a score based on IMT / halo size, we recommend a simple count of segments with positive halo sign ('halo count'). This count includes the right and left common superficial temporal arteries with their frontal and parietal branches (6 segments) and the axillary arteries (2 segments). The range of this score is 0-8	Rating 1-5
Q4. Statement: In case of missing segments (e.g. due to anatomical variants) all available segments will be considered. Segments biopsied before or during the study should be excluded. The score will then be divided by the number of evaluated segments and multiplied by the maximum number of segments, i.e. 8.	Rating 1-5
Q5. Statement: The IMT should be measured in the area of greatest thickness	Rating 1-5
Q6. Statement: The IMT should be measured in predetermined anatomical areas (e.g. 1 cm from the superficial temporal artery bifurcation and at the level of the humeral head)	Rating 1-5
Q7. Please rank order the statements of this page according to priority: • The IMT should be measured in the area of greatest thickness. • The IMT should be measured in predetermined anatomical areas (e.g. 1 cm from the superficial temporal artery bifurcation and at the level of the humeral head)	Rank ordering
Q8. Statement: When measuring the IMT at the point of greatest thickness the distance from the bifurcation of the superficial temporal artery and the distance from the mid of humeral head should be additionally noted.	Rating 1-5
Q9. Statement: The IMT / halo thickness of temporal and axillary arteries should be measured at the thickest wall (superficial or deep wall). At temporal arteries it may be an alternative to compress the vessel until no lumen or blood flow is visible with measurement of both walls dividing the result by 2.	Rating 1-5
Q10. Statement: The IMT / halo thickness of temporal arteries and axillary arteries should always be measured at the thickest wall (superficial or deep wall). Measurement of compressed temporal arteries should not be performed.	Rating 1-5
Q11. Statement: The IMT / halo thickness of temporal arteries and axillary arteries should always be measured at the deep wall. Measurement of compressed temporal arteries should not be performed.	Rating 1-5
Q12. Statement: The IMT / halo thickness of temporal and axillary arteries should always be measured with compression. The results will be divided by 2.	Rating 1-5
Q13. Statement: The IMT / halo thickness of temporal and axillary arteries should always be measured at the deep wall. At temporal arteries it may be an alternative to compress the vessel until no lumen or blood flow is visible with measurement of both walls dividing the result by 2.	Rating 1-5
Q14. Please rank order the statements of this page according to priority: • The IMT / halo thickness of temporal and axillary arteries should be measured at the thickest wall (superficial or deep wall). At temporal arteries it may be an alternative to compress the vessel until no lumen or blood flow is visible with measurement of both walls dividing the result by 2. • The IMT / halo thickness of temporal arteries and axillary arteries should always be measured at the thickest wall (superficial or deep wall). Measurement of compressed temporal arteries should not be performed.	Rank ordering

Step 3

- 信頼性の評価

Delphi法に参加したメンバーが,事前に1.5時間のオンライントレーニングを受けた.

各地から収集されたGCA治療前と治療4週間後の血管超音波所見をみてIMTを測定し,結果を記入.

2週間後に再度, 以前とは違う順番で画像を測定してもらい測定者内の一致を評価.

結果

欧州/アメリカ/アジアから49人の専門家が集まった.

- IMTのcut off値は, 浅側頭動脈 0.4mm, 頭頂枝/前頭枝 0.3mm, 腋窩動脈 1.0mm
- IMT rounded cut off values (OGUS)が採用.
- いわゆるHalo scoreは採用されず.
- 8領域でhalo singの有無を確認し, あれば合計していくhalo countの使用

Candidate ultrasonography scores for GCA					
1	*IMT-normal*: Sum of IMT measured in every segment divided by the mean normal IMT in each segment (common trunk of superficial temporal arteries, 0.23 mm; frontal branches, 0.19 mm; parietal branches, 0.20 mm; axillary arteries, 0.59 mm).				
2	*IMT-cut-off*: Sum of IMT measured in every segment divided by the cut-off values of IMT in each segment (common trunk of superficial temporal arteries, 0.42 mm; frontal branches, 0.34 mm; parietal branches, 0.29 mm; axillary arteries, 1.0 mm).				
3	*IMT-rounded normal*: Sum of IMT measured in every segment divided by the mean rounded normal IMT in each segment (all temporal artery segments, 0.2 mm; axillary arteries, 0.6 mm).				
4	*IMT-rounded cut-off*: Sum of IMT measured in every segment divided by the rounded cut-off values of IMT in each segment (common trunk of superficial temporal arteries, 0.4 mm; temporal artery branches, 0.3 mm; axillary arteries, 1.0 mm). *This score was finally selected as the provisional OMERACT GCA Ultrasonography Score (OGUS).*				
5	*Semiquantitative*: Calculated by the IMT measured in every segment. IMT is then converted into a semiquantitative value for each segment.[14]				
	Halo grading	**Common temporal IMT (mm)**	**Parietal branch IMT (mm)**	**Frontal branch IMT (mm)**	**Axillary artery IMT (mm)**
	Grade 0	≤0.3	≤0.2	≤0.1	≤0.5
	Grade 1	0.4	0.3	0.2	0.6
	Grade 2	0.5	0.4	0.3	0.7–0.8
	Grade 3	0.6–0.7	0.5	0.4	0.9–1.5
	Grade 4	≥0.8	≥0.6	≥0.5	≥1.6
6	*Halo count*: Sum of halos (absent=0, present=1) in every segment (range 0–8).[14]				

結果

OGUS=各領域のIMTを合計してcut off値で割ったものを合計, 測定可能な領域数で割ったもの.
0-1は正常, ＞1で異常

例:
浅側頭動脈 右 1.0mm, 左 0.5mm (合計 1.5mm)
前頭枝 右 0.5mm, 左 0.3mm (合計 0.8mm)
頭頂枝 右 0.3mm, 左 0.3mm (合計 0.6mm)
腋窩動脈 右 1.5mm, 左 1.0mm (合計 2.5mm)
[1.5/0.4+0.8/0.3+0.6/0.3+2.5/1.0]÷8=1.36

- OGUSが使用できないときは, halo countで代用する.
- 生検で動脈が使用できない時は,残りのIMTを合計して,実際に測定できたセグメントで割る.

Box 1 Provisional OMERACT GCA Ultrasonography Score (OGUS)

OMERACT GCA Ultrasonography Score (OGUS)=(CR/0.4 mm+CL/0.4 mm+PR/0.3 mm+PL/0.3 mm+FR/0.3 mm+FL/0.3 mm+AR/1.0 mm+AL/1.0 mm)/number of segments available.*
If OGUS cannot be determined, the *halo count*=Sum of all segments with a positive halo sign (range 0–8) may be used as *an alternative.*

OMERACT GCA Ultrasonography Score is calculated as the [Sum of intima–media thickness (IMT) measured in every segment divided by the rounded cut-off values of IMTs in each segment (ie, common trunk of superficial temporal arteries: 0.4 mm; parietal and frontal branches: 0.3 mm; axillary arteries: 1.0 mm)] divided by the number of segments available.
*In case one or more artery segments are not examined (eg, because of biopsy), the sum of the remaining segments (each divided by the rounded cut-offs) is divided by the number of segments actually available. This is to normalise the final score according to the number of segments investigated. In case the IMT has been measured on a compressed artery, the value has to be divided by 2 (see also box 2, statement 5).

結果

1.スコアには, 左右の側頭動脈総幹と前頭葉,頭頂枝(6),腋窩動脈(2)を含めるべき.

2. IMT/halo sizeに基づくスコアに加え, halo sign陽性の8セグメントを単純にカウントすることを推奨(halo count).

3. セグメントが欠落している場合(例：解剖学的変異など), 利用可能なすべてのセグメントで考慮する.生検されたセグメントは除外する.スコアは評価したセグメント数で割る.

4. IMTは最も厚みのある部位で測定.

5. 側頭動脈と腋窩動脈のIMT/Haloは, 最も厚い壁で測定される.

側頭動脈では, 内腔や血流が見えなくなるまで血管を圧迫し,両壁の測定結果を2で割るという方法もある

6. 測定はグレースケールで行うことが望ましい. 不明確な場合のみ, カラードップラーまたは血管内腔を示す別の超音波法を使って測定することができる

7. 測定値には少なくとも小数点以下1桁,可能であれば2桁を含めること.

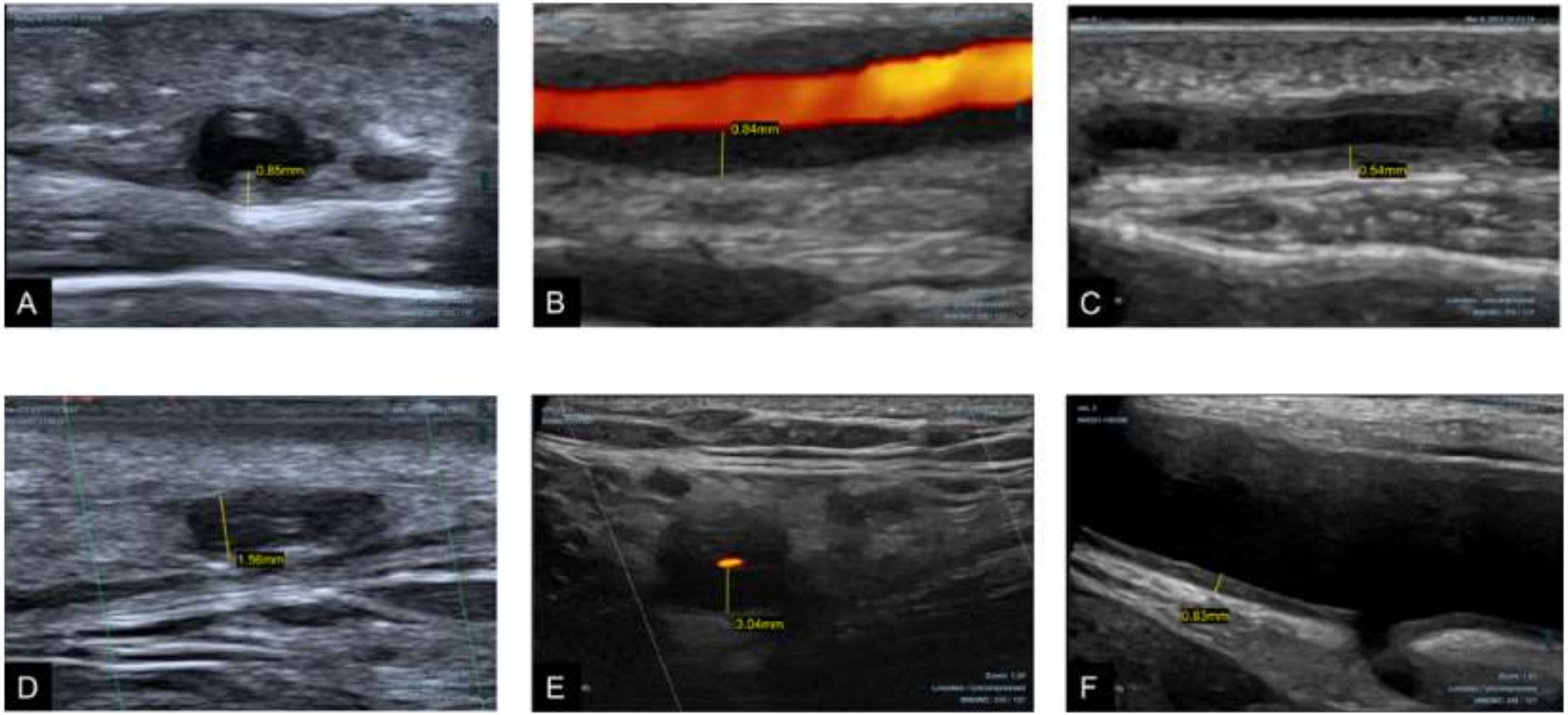
8. ベースライン時とフォローアップ時は可能であれば同じ方法を用いる.

9. IMTは,可能であれば縦断面で測定することが望ましい.

Box 2 Statements for the determination of the provisional OMERACT GCA Ultrasonography Score (OGUS)

1. The score should include the right and left common trunk of superficial temporal arteries with their frontal and parietal branches (six segments) and the axillary arteries (two segments) (agreement 91.3%, first Delphi round).
2. In addition to a score based on IMT/halo size, we recommend a simple count of segments with positive halo sign (halo count). This count includes the right and left common trunks of superficial temporal arteries with their frontal and parietal branches (six segments) and the axillary arteries (two segments) (agreement 79.6%, first Delphi round).
3. In case of missing segments (eg, due to anatomical variants), all available segments will be considered. Segments where a biopsy has been performed should be excluded. The score will then be divided by the number of evaluated segments (agreement 75.0%, first Delphi round).
4. The IMT should be measured in the area of greatest thickness (agreement 88.6%, first Delphi round).
5. The IMT/halo thickness of temporal and axillary arteries should be measured at the thickest wall (superficial or deep wall). At temporal arteries, it may be an alternative to compress the vessel until no lumen or blood flow is visible with measurement of both walls dividing the result by 2 (agreement 75.0%, first Delphi round).
6. Measurement should preferably be performed in the grey scale image. Only in unclear situations measurement may be done using colour Doppler ultrasonography or an alternative ultrasonography mode for showing the artery lumen. Overfilling or underfilling of the lumen with colour must be avoided in this situation (agreement 93.0%, first Delphi round).
7. Measurements should include at least one, but if possible two decimal places (agreement 85.1%, second Delphi round).
8. At baseline and follow-up, the same method (single wall measurement or measurement with compression) should be applied if possible (agreement 87.2%, second Delphi round).
9. IMT should preferably be measured in longitudinal planes, if possible (agreement 89.1%, third Delphi round).

測定の例



結果

◆Reliability Exercise

WG 9名が57症例の超音波画像を提供
GCA 16例とコントロール7例が抽出.

- IMT測定の検者内ICCは1回目 0.835, 2回目 0.724, 検者間ICC 0.911と良好
- Halo countの検者内ICCは1回目 0.562, 2回目 0.565, 検者間ICC 0.885と悪化

Table 2 Reliability data for the candidate ultrasonography scores for GCA

	Interrater Round 1		Interrater Round 2		Intrarater	
Score	ICC	95% CI	ICC	95% CI	Median ICC	IQR
IMT-normal	0.837	0.684 to 0.951	0.719	0.526 to 0.906	0.913	0.752–0.955
IMT-cut-off	0.832	0.676 to 0.949	0.718	0.525 to 0.905	0.912	0.753–0.952
IMT-rounded normal	0.840	0.688 to 0.952	0.718	0.525 to 0.905	0.915	0.750–0.956
IMT-rounded cut-off (OGUS)	**0.835**	**0.681 to 0.950**	**0.724**	**0.532 to 0.907**	**0.911**	**0.752–0.953**
Semiquantitative	0.540	0.396 to 0.712	0.557	0.417 to 0.722	0.889	0.740–0.931
Halo count	0.562	0.420 to 0.730	0.565	0.427 to 0.727	0.885	0.771–0.922

結果

- PROTEA studyでOGUSとHalo countの外的妥当性を評価
  - OGUSは24wのSMD -1.69でvery large effectに相当
  - Halo countは24wのSMD -1.62でvery large effectに相当
  - IMT-normal, IMT-cut-off, IMT-rounded normal, Halo scoreもSMDがmedium effectであり, それなりに良好.
  - OGUSは, CRP/ESR,BVASとも中程度で相関する.

Table 4 Correlation between candidate ultrasonography scores and markers of disease activity using data from the Prognosis of Temporal Arteritis (PROTEA) study

	Correlation coefficient			OR
	ESR*	CRP*	BVAS	Disease remission
IMT-normal	0.48	0.43	0.37	0.34 (0.18 to 0.64)
IMT-cut-off	0.48	0.43	0.37	0.34 (0.18 to 0.63)
IMT-rounded normal	0.48	0.43	0.37	0.34 (0.18 to 0.64)
IMT-rounded cut-off (OGUS)	**0.48**	**0.43**	**0.37**	**0.34 (0.18 to 0.63)**
Semiquantitative	0.38	0.29	0.23	0.46 (0.28 to 0.76)
Halo count	0.45	0.36	0.28	0.43 (0.28 to 0.66)

The results are reported as correlation coefficients between 24-0 weeks score variations and 24-0 weeks variations of ESR, CRP and BVAS, and as ORs for remission.
The magnitude of the correlation may be interpreted as follows: small: (0.10–0.30); moderately: (0.30–0.50); large: (0.50–0.70); very large: (0.70–1.00). All correlation coefficients are statistically significant with p<0.001 (not corrected for multiple testing).

Table 3 Sensitivity to change of the candidate ultrasonography scores using data from the Prognosis of Temporal Arteritis (PROTEA) study

	Week 1 (n=52)	Week 3 (n=42)	Week 6 (n=43)	Week 12 (n=38)	Week 24 (n=39)
IMT-normal	−1.21	−1.43	−1.42	−2.18	−1.70
IMT-cut-off	−1.16	−1.41	−1.40	−2.17	−1.69
IMT-rounded normal	−1.20	−1.44	−1.42	−2.21	−1.69
IMT-rounded cut-off (OGUS)	**−1.19**	**−1.42**	**−1.41**	**−2.16**	**−1.69**
Semiquantitative	−0.81	−1.11	−1.35	−2.23	−1.67
Halo count	−0.51	−0.81	−1.18	−1.73	−1.62

The standardised mean difference (SMD) of interest is reported as negative values and in units of standard deviations indicating the magnitude of change between baseline and different time points. The values may be interpreted as follows: no effect: (−0.2, 0), small effect: (−0.5 to −0.2); medium effect: (−0.8 to −0.5); large effect: (−1.3 to −0.8); very large effect: (−∞, −1.30).

考察

- 薬剤がCRP/ESRに影響を及ぼすため, 疾患活動性や治療効果判定の指標が必要であった.
- このスコアは, 研究, 特に薬理学的介入の有効性を検証する試験で疾患活動性のMonitoring toolおよび治療効果判定として使用することができる。

- semiquantitative score, いわゆるHalo scoreは選ばれなかった.
- 信頼性,感度の検証, 収束的妥当性がOGUSより劣っていた可能性がある.
- Halo scoreはモニタリングより診断目的や層別化のツールとして使われ, OGUSは臨床試験のMonitoringやOutcomeのパラメーターとして使われるかもしれない.
- Halo scoreの欠点は, IMTが正常範囲でもスコアが上昇することや, 生検後や解剖学的に欠損している例の取り扱いが不明確.

考察

Strength

- 世界中から専門家が参加
- 信頼性の検査が行われた
- 他のコホートで感度を検証
- 収束的妥当性を検証

Limitation

- 信頼性試験は, 静止画像で行われており実際の患者で評価していない.
- RCTで検証していない.
- IMTが測定できない患者が一定数存在し,スコアのばらつきが大きい.
- 感度を検証したPROTEA研究は, 標治療介入の有効性を検証するための試験で, 参加前にPSLが使用された.
- PROTEA試験は頭蓋内血管の患者が多く, 頭蓋外の血管に所見がある場合の有効性は不明.
- 活動性と寛解時のスコアのカットオフ値や臨床的な効果を示すΔ値は不明.
- 8領域以外の血管に炎症がある場合は使用できない.