increased cardiovascular risk in mixed connective tissue disease: evaluation of macrovascular involvement and its predictors by aortic pulse wave velocity

1 Konstantinos Triantafyllias, Michele De Blasi1, Freya Lütgendorf1, Lorenzo Cavagna4, Marco Stortz3, Julia Weinmann-Menke3, Stavros Konstantinides4, Peter Galle5, Andreas Schwarting3, Anja van Roon1, Alja J. Stel2, Hendrika Bootsmaw, Andries Smit1, Douwe J. Mulder 1.

Background: Macrovascular involvement and cardiovascular (CV) risk have not been sufficiently studied in patients with mixed connective tissue disease (MCTD). In particular, the gold standard assessment method of aortic stiffness carotid-femoral pulse wave velocity (cfPWV) has never been evaluated in patients with this disease.

Objectives: Aims of the present study were to examine cfPWV in MCTD and to evaluate its associations with MCTD associated parameters and traditional CV risk factors.

Methods: cfPWV measurements were performed in 43 MCTD patients and 107 healthy controls. The difference between cfPWV in the two groups was statistically examined and subsequently controlled for the effect of possible confounding factors. Association of cfPWV with MCTD associated organ involvement, routine laboratory parameters and immunoserological markers was also evaluated. Finally, relationship of cfPWV with medications and traditional CV risk factors was examined.

Results: Adjusted statistical analyses for confounding factors showed significantly higher cfPWV values in MCTD patients in comparison to controls (rho\textsubscript{adj}=0.001). cfPWV correlated in both the patients and the control group significantly with age (rho\textsubscript{adj}=0.69, p<0.001 and rho\textsubscript{adj}=0.67, p=0.001 respectively), diastolic arterial pressure (rho\textsubscript{adj}=0.024 and p=0.032 respectively) and mean arterial pressure (rho\textsubscript{adj}=0.44, p=0.004 and rho\textsubscript{adj}=0.49, p=0.001 respectively). Moreover, cfPWV was higher in the control group with systolic arterial pressure (p=0.001) (Fig. 1). Higher cfPWV values could be documented in the subset of MCTD patients without lung involvement (p=0.049).

Conclusion: To our knowledge, this is the first study to show that patients with MCTD have significantly higher aortic stiffness and thus CV risk in comparison to controls. Except the disease itself, age and blood pressure were the main predictors of cfPWV.

REFERENCES

Disclosure of Interests: None declared.


ASSESSING RECOVERY TIME AFTER COLD CHALLENGE AND THUMB INVOLVEMENT CAN HELP TO RULE OUT SYSTEMIC SCLEROSIS IN PATIENTS PRESENTING WITH RAYNAUD’S PHENOMENON

1 Annie van Roon1, Arie Van Roon1, Alja J. Ste2, Hendrika Bootsmaw, Andries Smit1, Douwe J. Mulder1, 2University of Groningen, University Medical Center Groningen, Internal Medicine, division Vascular Medicine, Groningen, Netherlands; 3University of Groningen, University Medical Center Groningen, Rheumatology and Clinical Immunology, Groningen, Netherlands

Background: Distinguishing primary Raynaud’s phenomenon (PRP) from Raynaud’s phenomenon secondary to systemic sclerosis (SSc) is crucial in the early detection of SSc. Recently we reported that patients with more severe vasculopathy suffer from a prolonged ischemia time during Raynaud’s attack. [1] Additionally, it appears that the thumb is more frequently involved in SSc, where it seems to be spared in PRP. [2] These two characteristics are easily recognized by patients and physicians, and can help rising awareness for SSc.

Objectives: The aim was to study if the recovery of a Raynaud’s attack and involvement of the thumb are differentiators for SSc in patients with Raynaud’s phenomenon (RP).

Methods: A stepwise cooling and recovery procedure was performed, provoking an RP attack, in patients with PRP and SSc. One hand was submerged up till the radiocarpal joint in water. The water temperature was lowered in steps of 3 degrees Celsius every four minutes, from 33 until at least 9 degrees Celsius. Afterwards ten minutes of recovery in room air of 23 degrees Celsius was observed. During the procedure perfusion of the fingertips was assessed by photo-electric plethysmography.

Results: In total 18 patients with SSc and 68 patients with PRP underwent the procedure. Seventeen (94%) SSc patients had no restoration of perfusion after ten minutes in one or more fingers, compared to 28 (41%) PRP patients (figure 1), with a negative predictive value of 98%. During cooling, 17 (94%) SSc patients developed abnormal perfusion in the thumb compared to 48 (71%) PRP patients (p=0.036), with a negative predictive value of 95%. There was no difference in involvement of the other fingers during cooling (all p>0.05). Positive predictive values were low.

Conclusion: In patients with RP, when there is restoration of perfusion in all fingers after ten minutes or when the thumb is spared, the presence of an underlying SSc is very unlikely. Although this objective measurement needs to be verified with patient’s reports, these results suggest that these simple signs can help physicians to assess if the patient needs to be referred for additional tests.
REFERENCES

Disclosure of Interests: Anniek van Roon: None declared, Arle Van Roon: None declared, Alja J. Stel: None declared, Hendrika Bootma Grant/research support from: Unrestricted grants from Bristol-Myers Squibb and Roche, Consultant for: Roche, Bristol-Myers Squibb, Novartis, Medicom, Union Chimique Belge, Speakers bureau: Bristol-Myers Squibb, Novartis, Andries Smit Shareholder of: Has been co-founder, and is still shareholder of Diagnostics Technologies, the company which developed the AGE reader., Douwe J Mulder Grant/research support from: Unrestricted grants from Bristol-Myers Squibb and Roche, Andries Smit Shareholder of: Has been co-founder, and is still shareholder of Diagnostics Technologies, the company which developed the AGE reader., Douwe J Mulder Grant/research support from: My University has received research grants for my research from: Sanofi

Table 1: Validation of durometry according to the OMERACT Filter 2.0

<table>
<thead>
<tr>
<th>Pillar</th>
<th>Subdomain</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Truth</td>
<td>Face validity</td>
<td>[1]</td>
</tr>
<tr>
<td></td>
<td>Content validity</td>
<td>[4]</td>
</tr>
<tr>
<td></td>
<td>Construct validity</td>
<td>[4, 5]</td>
</tr>
<tr>
<td>Discrimination</td>
<td>Sensitivity to change in a context of a RCT</td>
<td>[1]</td>
</tr>
<tr>
<td></td>
<td>Discrimination between changes in situations of change</td>
<td>[1, 3, 6]</td>
</tr>
<tr>
<td></td>
<td>Stability of situations of no change</td>
<td>[1, 3]</td>
</tr>
</tbody>
</table>

Feasibility
- a criterion was judged valid, if appropriate evidence from studies including SSc patients indicated that durometry met the requirements to be valid
- a criterion was judged partially valid, if appropriate evidence from studies including SSc patients indicated that durometry only partially met the requirements to be valid
- a criterion was judged invalid, if no evidence from studies including SSc patients was found

Conclusion: Current systematically identified evidence suggests partial validation of durometry in SSc patients according to the OMERACT Filter 2.0. Further dedicated studies are needed to completely validate this tool in SSc, more specifically concerning the pillar discrimination.

REFERENCES

Disclosure of Interests: None declared


AB0694

IS DUROMETRY A RELIABLE TOOL TO INVESTIGATE SKIN HARDINESS IN SYSTEMIC SCLEROSIS? A PILOT STUDY AND SYSTEMATIC LITERATURE REVIEW

Amber Vanhaecke1, Maurizio Cutolo2, Sven Verschuere1, Greta Pacini1, Veronica Vilela3,4, Vanessa Smith5,6, Ghent University, Department of Internal Medicine, Ghent, Belgium; 2Ghent University Hospital, Department of Rheumatology, Ghent, Belgium; 3IRCCS San Martino Polyclinic Hospital, University Of Genoa, Research Laboratory And Academic Division Of Clinical Rheumatology, Department Of Internal Medicine, Genoa, Italy; 4VIB Inflammation Research Center (IRC), Unit for Molecular Immunology and Inflammation, Ghent, Belgium

Background: Fibrosis represents one of the main characteristics of systemic sclerosis (SSc), with skin and internal organ involvement being its main clinical expressions. The modified Rodnan Skin Score (mRSS), using clinical palpation to estimate skin thickness, is considered the current “gold standard” to measure skin involvement in a semi-quantitative way. The mRSS has been judged as fully validated through the Outcome Measures in Rheumatology Clinical Trials (OMERACT) Filter, however a high risk of observer bias exists. Therefore, a new challenge for the SSc community is to define a reliable tool, able to more precisely investigate skin involvement in SSc patients, which would be of great value in clinical trials. Durometry, to define a reliable tool, might address this need.

Methods: Relevant full-text articles using durometry in SSc patients were identified through a systematic literature search in PubMed, EMBASE and Web of Science, according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Besides this systematic search, an additional hand search was performed through reference list screening. All retrieved records were screened by two raters based on title, abstract and full-text level to finally include manuscripts eligible for quality appraisal and data extraction. The finally included manuscripts were analysed according to the OMERACT Filter 2.0.

Results: The systematic search yielded 94 records, of which 50 were unique. Seven records were retained for full-text review and analysis, comprising one randomised clinical trial (RCT). The pillar feasibility was well documented in 3 studies [1-3]. Of note, the credibility (i.e. having face validity) of durometry was considered to be valid, as was stated by Kissin et al [1]. Concerning the (pillar) truth: content validity was confirmed as durometry correlated well with histological findings (i.e. myofibroblast score and hyalinized collagen, r=0.69 and 0.78 respectively) [4], construct validity was confirmed as a moderate to high significant correlation with the total mRSS was documented in 5 studies (correlation coefficients ranging 0.59-0.81) [1, 3-6]. Concerning the pillar discrimination, the sensitivity to change in the context of one RCT was confirmed [3], inter-rater reliability was confirmed as intra-class correlation coefficients (ICC) ranged from 0.61-0.91 in 2 studies, of which one RCT [1, 3], intra-rater reliability has not been confirmed as this was domain was only investigated in a cohort 5 SSc patients (ICC 0.86-0.94) and thus solid evidence was lacking [1]. The sensitivity to change in situations of change (i.e. change over time, discrimination between SSc patients or between SSc patients and controls) was not confirmed, since solid evidence was lacking in literature.

Conclusion: Current systematically identified evidence suggests partial validation of durometry in SSc patients according to the OMERACT Filter 2.0. Further dedicated studies are needed to completely validate this tool in SSc, more specifically concerning the pillar discrimination.

REFERENCES

Disclosure of Interests: None declared