Background: Giant cell arteritis (GCA) is a systemic inflammatory vasculitis that often presents with headaches and visual symptoms. It is a medical emergency as it can lead to permanent sight loss. Prompt treatment with high doses of glucocorticoid therapy is often required. However, it has been shown that GCA patients on glucocorticoid therapy develop muscle weakness, known as glucocorticoid induced myopathy (1).

Quantitative MRI may be sensitive to detect the differences in muscle parameters between newly diagnosed GCA patients compared to healthy controls. MRI T2 is sensitive to fluid related to physiological changes at the molecular level, and is regarded as an indirect measure of muscle inflammation (2). MRI muscle fat fraction (FF) is useful for identifying myosteatosis (3). Diffusion tensor imaging (DTI) is sensitive to changes in muscle microstructure and may be useful in identifying changes to muscle fibres (4).

Objectives: To obtain preliminary estimates of the extent to which quantitative MRI-based measurements of muscle T2, FF, DTI and volume differ between newly diagnosed GCA patients and healthy controls (HC) and how the muscle changes over 3- and 6-month intervals following glucocorticoid therapy.

Methods: MRI of the mid-thigh were acquired using Dixon imaging to assess FF, and isometric dynamometer to measure grip strength.

Results: 20 GCA patients (68.2±8.3 years, 14/20 female, mean ESR 26.9mm/h, mean CRP 39.6mg/L) were enrolled within 14 days of starting glucocorticoids: 15 returned at 3 months (mean ESR 17mm/h, mean CRP 5.7mg/L); 8 returned at 6 months (mean ESR 18mm/h, mean CRP 6mg/L). 20 directly age- and gender-matched HC also were recruited. T2, FF and HF were higher and muscle volume lower in the GCA patients at baseline compared to HC (fig 1 and 2). Within the hamstrings, the mean differences between GCA patients and HC for T2, FF and muscle volume were 2.2ms (95% CI 1, 4; p=0.09), 3.8% (95% 2, 5; p<0.001), and -166cm³ (95% CI 110, 210; p<0.001) respectively. There was no substantive difference in mean diffusivity or fractional anisotropy. Results in the quadriceps followed a similar trend. Following glucocorticoid treatment, there were no substantive changes in MRI measurements. Knee flexion/extension and handgrip strength were lower in the GCA patients at baseline compared to HC, with differences of -5.3Nm (95% CI 32.6, -7.7; p=0.003) and -4.4Nm (95% CI -56.7, -1.3; p=0.04) for flexion and extension respectively. Muscle strength did not change following glucocorticoid treatment.

Conclusion: This pilot study suggests for the first time that muscle health may be affected in newly diagnosed GCA patients compared to age and gender matched HC, as demonstrated by higher T2 and FF, and lower muscle volume and muscle strength. These preliminary results show that muscle changes may occur in the early stages of GCA and persist throughout the disease duration. If these findings are confirmed, it will be important to consider interventions to improve muscle health in the treatment pathway for GCA.

References:

Figure 1. Quantitative MRI measurements of GCA patients and healthy controls in the hamstrings.

Figure 2. Quantitative muscle volume and muscle strength measurements of GCA patients and healthy controls.

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CLINICAL UTILITY OF TESTING CONVENTIONAL AND NON-CONVENTIONAL ANTI-PHOSPHOLIPID ANTIBODIES IN SUSPECTED OBSTETRIC ANTI-PHOSPHOLIPID SYNDROME

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Background: Anti-phospholipid syndrome (APS) is an important cause for recurrent pregnancy losses (RPL), Conventional APS antibodies (aPLs) like lupus anti-coagulant (LA), anti-cardiolipin (ACL) and anti-beta 2 glycoprotein I (anti-β2 GP I) are not present in significant number of obstetric APS(OAPS) patients, leading to a state described as “séro-negative” OAPS (SNOAPS). Recent literature shows non-conventional aPLs like Anti phosphatidylserine-prothrombin complex (Anti-PSPT) and Anti-Annexin V (Anti-Ann V) can be positive in up to 50% of SNOAPS patients.

Objectives: Testing the performance of conventional and non-conventional aPLs in suspected OAPS patients (obstetric events as defined in the Sydney classification criteria for APS)

Methods: We performed a retrospective chart review of 101 patients who underwent combined testing for non-conventional aPLs for suspected OAPS from May 2016 to November 2019 at our department. Patients were categorized into OAPS cases (n=50, median age 31 years) and controls (n=51, median age 30 years) based on their fulfillment of clinical definition of OAPS events defined by Sydney criteria. Conventional aPLs were tested by methods adapted in Sydney criteria and Anti PSPT / Anti Ann V were tested by commercial ELISA. The sample size (n=101) has 95% confidence interval with a margin of error of 10% for the objective of the study.
Results: 36 cases (72%) were ‘sero-positive’ & 14 cases (28%) were truly ‘sero-negative’ for conventional aPLs. 5 (35.7%) of the SNOAPS patients were positive for Anti-PSPT and/or Anti AnnV antibodies. Performance of the various aPLs in suspected OAPS is displayed in Table 1 & Figure 1.

Table 1 showing the performance of the various conventional and non-conventional aPLs in suspected obstetric APS cases

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Likelihood</th>
<th>Predictive</th>
<th>Positive</th>
<th>Negative</th>
<th>Accuracy</th>
<th>Youden’s Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>LA</td>
<td>50%</td>
<td>94.1%</td>
<td>8.5</td>
<td>0.5</td>
<td>89.3%</td>
<td>65.7%</td>
<td>72.3%</td>
<td>44.1%</td>
</tr>
<tr>
<td>ACL</td>
<td>32%</td>
<td>98%</td>
<td>16.3</td>
<td>0.7</td>
<td>94.1%</td>
<td>59.5%</td>
<td>65.3%</td>
<td>30%</td>
</tr>
<tr>
<td>anti II GP I IgM</td>
<td>38.4%</td>
<td>91.4%</td>
<td>4.5</td>
<td>0.7</td>
<td>83.3%</td>
<td>57.1%</td>
<td>63.5%</td>
<td>29.7%</td>
</tr>
<tr>
<td>anti II GP I IgG</td>
<td>24%</td>
<td>96.1%</td>
<td>6.1</td>
<td>0.8</td>
<td>85.7%</td>
<td>66.4%</td>
<td>60.4%</td>
<td>20.1%</td>
</tr>
<tr>
<td>Anti PSPT</td>
<td>28%</td>
<td>96.1%</td>
<td>7.1</td>
<td>0.7</td>
<td>87.5%</td>
<td>75.6%</td>
<td>62.4%</td>
<td>24.1%</td>
</tr>
<tr>
<td>Anti AnnV</td>
<td>28%</td>
<td>98%</td>
<td>14.3</td>
<td>0.7</td>
<td>93.3%</td>
<td>58.1%</td>
<td>63.4%</td>
<td>26%</td>
</tr>
<tr>
<td>Conventional</td>
<td>72%</td>
<td>88.2%</td>
<td>6.1</td>
<td>0.3</td>
<td>85.7%</td>
<td>76.3%</td>
<td>79.8%</td>
<td>60.2%</td>
</tr>
<tr>
<td>APLS Non-conventional</td>
<td>38%</td>
<td>94.1%</td>
<td>6.4</td>
<td>0.7</td>
<td>86.4%</td>
<td>60.7%</td>
<td>66.3%</td>
<td>32.1%</td>
</tr>
<tr>
<td>APLS All APLS</td>
<td>82%</td>
<td>86.3%</td>
<td>6.00</td>
<td>0.20</td>
<td>85.4%</td>
<td>84.3%</td>
<td>84.2%</td>
<td>68.3%</td>
</tr>
</tbody>
</table>

Figure 1 showing the comparative diagnostic performance of Conventional aPL testing vs Combined testing along with non-conventional aPLs in suspected obstetric APS scenario

Conclusion: In a delicate situation like RPL, performance of non-conventional aPLs on their own, though not as sensitive as conventional aPLs, still demonstrate better specificity. Non-conventional aPLs can newly identify 1/3rd of SNOAPS as APS. The real value of testing Anti PSPT & Anti Ann V in RPL, is combined testing with conventional aPLs wherein they improve the sensitivity and accuracy of diagnosis of OAPS by 10% & 4.4 % respectively, with only 1.9% drop in specificity. Non-conventional aPLs should be tested in SNOAPS.

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Figure 1. Anatomical sites of US evaluation: joints, enthesis and tendons

Methods: PsA (CASPAR criteria) [1], PsO with MSK symptoms without fulfilling CASPAR criteria (symptOspO) and PsO with no MSK symptoms (asymptoPsO) were included. Socio-demographic characteristics, comorbidities, disease duration and treatment were collected. All patients underwent to: a) dermatological and rheumatologic assessment: PsO severity, swollen joint count (SJC), tender joint (TJC), number of dactylitis and enthesitis; b) US evaluation of joints, tendons and entheses according to OMERACT definitions[2], (figure 1); c) PROs assessment: fatigue, disability (HAQ) and QoL (SF36). Variables were compared across groups (chi square or one-way ANOVA test). Correlations were evaluated using Spearman’s test.

Results: 208 patients (76 PsA, 64 symptoPsO and 68 asymptoPsO) with similar socio-demographic characteristics and PsO duration were included (table 1).

Except for entheseopathies, all US changes were significantly higher in PsA, followed by symptoPsO patients.

Across all 3 groups, all PROs correlated mainly with demographic variables, comorbidities, TJC, clinical enthesis, skin severity, depression and fibromyalgia points (r=0.24-0.72). SymptoPsO and PsA reported similar scores of fatigue and impact on most QoL domains, significantly higher than asymptoPsO. HAQ correlated with total number of joints with US irregularities/osteophytes in PsA (r= 0.23; p=0.05), and SF36 physical function with both US inflammatory and structural damage variables in all three groups (r=0.24-0.34).

Conclusion: Quality of life, disability and fatigue were more impaired in PsA and symptoPsO patients than asymptoPsO. In all groups, PROs seem to be mostly associated with socio-demographic characteristics and comorbidities rather than objective measures such as US changes or clinical variables.

References: