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Rheumatic & Musculoskeletal Diseases

ORIGINAL RESEARCH

Remote self-collection of capillary blood using upper arm devices for autoantibody analysis in patients with immune-mediated inflammatory rheumatic diseases

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ABSTRACT

Objectives To evaluate the feasibility, accuracy, usability and acceptability of two upper arm self-sampling devices for measurement of autoantibodies and C reactive protein (CRP) levels in patients with immune-mediated rheumatic diseases (IMRDs).

Methods 70 consecutive patients with IMRD with previously documented autoantibodies were assigned to supervised and unsupervised self-collection of capillary blood with the Tasso+ or TAP II device. Interchangeability of 17 biomarkers with standard venesection was assessed by: concordance, correlation, paired sample hypothesis testing and Bland-Altman plots. Patients completed an evaluation questionnaire, including the System Usability Scale (SUS) and Net Promoter Score (NPS).

Results While 80.0% and 77.0% were able to safely and successfully collect capillary blood using the Tasso+ and TAP II within the first attempt, 69 of 70 (98.6%) patients were successful in collecting capillary blood within two attempts. Concordance between venous and capillary samples was high; 94.7% and 99.5% for positive and negative samples, respectively. For connective tissue disease screen, anti-Ro52 and anti-proteinase 3 autoantibody levels, no significant differences were observed. Self-sampling was less painful than standard venesection for the majority of patients (Tasso+: 71%; TAP II: 63%). Both devices were well accepted (NPS; both: +28%), usability was perceived as excellent (SUS; Tasso+: 88.6 of 100; TAP II: 86.0 of 100) and 48.6%/62.9% of patients would prefer to use the Tasso+/TAP II, respectively, instead of a traditional venous blood collection.

Conclusions Remote self-collection of capillary blood using upper arm-based devices for autoantibody and CRP analysis in patients with autoimmune rheumatic diseases is feasible, accurate and well accepted among patients.

Trial registration number WHO International Clinical Trials Registry (DRKS00024925).

WHAT IS ALREADY KNOWN ON THIS SUBJECT

⇒ Remote care can improve the referral process to rheumatology and monitoring of chronic diseases.
⇒ Autoantibody analysis is essential to establish the correct diagnosis and provide adequate disease monitoring in rheumatology.

WHAT THIS STUDY ADDS

⇒ Capillary blood self-sampling is promising, as it seems feasible, reliable and well accepted by a variety of patients with rheumatic diseases.
⇒ This is the first study investigating at-home self-sampling for autoantibody analysis and comparative performance of two different upper arm devices.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Implementation of capillary blood self-sampling could improve current rheumatology clinical pathways by empowering patients, reducing overall burden and costs.

INTRODUCTION

Immune-mediated rheumatic diseases (IMRDs), such as systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), Sjogren's syndrome, systemic vasculitis, idiopathic inflammatory myositis and systemic sclerosis, are often causing unspecific symptoms. For patients,[1] general physicians[2] and even rheumatologists,[3] these symptoms are difficult to correctly attribute. Once an IMRD is suspected, the presence of specific autoantibodies and elevated inflammatory markers often prompts rheumatology referral, enabling a precise and rapid diagnosis.[3] The importance of autoantibodies such as double-stranded DNA (dsDNA)

for the diagnosis of SLE is highlighted by their inclusion in American College of Rheumatology/EULAR disease classification criteria.[4] Similarly, serological biomarkers such as C reactive protein (CRP) are part of gold-standard composite scores to longitudinally monitor disease activity, such as the 28-joint Disease Activity Score-CRP[5] for RA and the Ankylosing Spondylitis Disease Activity Score-CRP (ASDAS-CRP) for spondyloarthritis.[6] Additionally, an increasing number of publications emphasise the value of autoantibody levels such as dsDNA,[7] proteinase 3 (PR3)[8] or myeloperoxidase (MPO)[9] as predictive surrogate parameters for disease activity and flares.

The COVID-19 pandemic caused a sudden decline of face-to-face visits[10] and rapid uptake of telemedicine.[11] Patients are increasingly using digital symptom checkers to quickly assess new symptoms and receive disease suggestions[11 12]; however, the accuracy of these largely symptom-based tools is low.[13–15] Likewise, remote patient monitoring was increasingly being adopted, via video consultations[16] and electronic patient-reported outcomes (PROs).[17] As anticipated by Burmester in a futuristic outlook of Rheumatology 4.0,[18] decentralised collection of blood could become a major cornerstone of telerheumatology[19] and is desired by a large proportion of patients with rheumatic disease.[11 19] Self-collection of blood became an unquestionable part of anticoagulation management[20] and has revolutionised diabetes management.[21] Although promising, the publications regarding blood self-collection in rheumatology remain scarce.[22–25] Previous trials shed light on the potential for monitoring drug levels of adalimumab[23] and hydroxychloroquine,[24] PRIME cell-based[22] and CRP-based[25] flare prediction. All of these studies used traditional finger-prick (FP)-based samples.

New upper arm (UA)-based semiautomated self-collection devices, such as the Tasso+ and TAP II, however, promise easier usage, more blood volume and less pain.[26–28] In a recent randomised controlled trial, we compared conventional FP-based sampling with UA-based sampling using the TASSO-serum separation tube (SST) device. We demonstrated that self-sampling provides accurate results for IgM rheumatoid factor (RF IgM), anti-cyclic citrullinated protein antibodies (anti-CCP IgG) and CRP, and both techniques were significantly less painful compared with professional venous blood collection. Patients clearly preferred UA devices, compared with finger-pricking to collect blood at home (60% for UA vs 32% for FP).[29] The study was limited to these three biomarkers and a supervised setting at the hospital.

In line with EULAR's research agenda for patient self-management[30] and remote care,[31] we aimed to evaluate the accuracy, feasibility, usability and acceptability of two UA self-sampling devices (Tasso+ and TAP II) in patients with IMRD for measurement of autoantibodies and CRP levels.

METHODS

Study design

This prospective study was registered in the WHO International Clinical Trials Registry (DRKS00024925). Three official patient partners from the largest German patient organisation were involved in the design of the study and discussion of the results (GB, MK, CE-A; Deutsche Rheuma-Liga Bundesverband e.V.). All patients provided written informed consent to participate in the study. Study results were reported following the STAndards for the Reporting of Diagnostic accuracy studies guideline.[32]

Study flow and blood collection

Consecutive patients with IMRD with previously documented autoantibodies were recruited from the inpatient and outpatient clinics of the Department of Rheumatology at the University Hospital Erlangen. Figure 1 depicts the study flow. The study consisted of two consecutive phases, in which patients underwent a traditional venous blood collection (gold standard), a first supervised capillary blood collection, followed by an evaluation questionnaire and a second capillary blood collection.

During each study phase, patients were alternately allocated to the two blood collection devices: Tasso+ (Tasso, Seattle, Washington, USA) or TAP II (YourBio Health, Medford, USA) (see figure 2). Both capillary blood self-collection devices are self-adhesive and adhered to the UA. Tasso+ is lancet based, whereas TAP II uses multiple micro-needles to puncture the skin.

Patients were given access to printed blood collection instructions and publicly available English instruction videos (Tasso+: https://www.tassoinc.com/tasso-plus; TAP II: https://bit.ly/3HCngxK). If preferred by the patient, the original audio track in English was muted, while the instructions displayed in the video were simultaneously explained in German. Any deviations from the instructions were registered by study personnel during the supervised capillary blood collections. Study personnel did not answer any questions and only intervened in case of potential harm of patients.

Prior to blood collection, patients were instructed to apply a heat pad for 3 min to the respective blood sampling site to promote vasodilation. After disinfecting the skin with an alcohol wipe, the blood collection devices were attached to the UA by an adhesive and activated by pressing a button. After activation and consecutive skin puncture, the devices applied a vacuum to automatically collect blood into an attached tube. Tasso+ devices used 2 mL BD Microtainers, golden cap and SSTs to collect the capillary whole blood, while TAP II devices used RAM Scientific, red cap, clot activator and gel tubes. The capillary blood collection was therefore limited to a maximum of approximately 1 mL whole blood.

Venous samples and matched samples of the first supervised capillary blood collection were kept at room temperature for at least 30 min, then centrifuged for 15 min at 3200 RPM stored at 4°C until shipped to Thermo Fisher Scientific (Freiburg, Germany) for analysis.
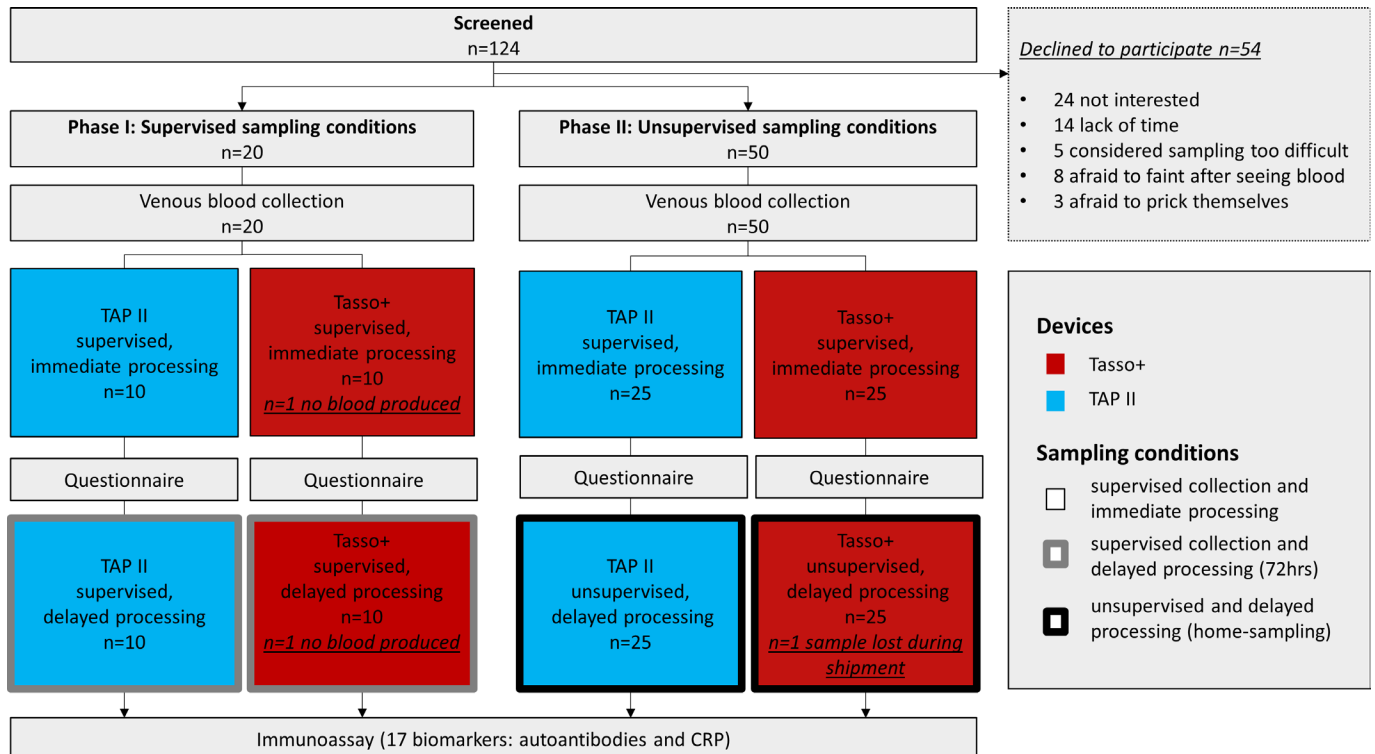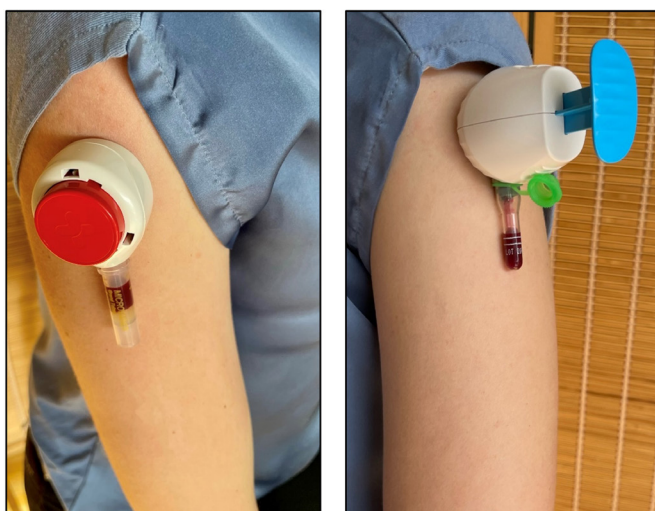
Figure 1 Patient flow diagram. CRP, C reactive protein.

During study phase 1, 10 patients per device carried out a second supervised capillary blood collection, which was centrifuged after incubation for 72 hours at uncontrolled room temperature to analyse sample stability. The consecutive 50 patients (25 per device) received blood collection kits and postage packages to independently carry out a second blood collection (unsupervised) within 1 week of the appointment during study phase 2.

Autoantibody and CRP analysis

Upon arrival in the laboratory, the resulting serum volume was measured, sample quality assessed, serum

Figure 2 Capillary blood upper arm self-collection devices.

samples were transferred into fresh Sarstedt 2 mL Polypropylene Micro Tubes (Sarstedt AG & Co, Nümbrecht, Germany) and stored at −20°C until analysis. CRP was determined using Thermo Scientific Indiko Plus Clinical Chemistry Analyzer (Dreieich, Germany). The autoantibodies were measured on the Phadia 250 and 2500 instruments using the following fluorescence enzyme immunoassay-based tests (EliA, Thermo Fisher Scientific, Phadia AB, Sweden): EliA connective tissue disease (CTD) screen (antigens: human recombinant U1RNP (RNP70, A, C), SS-A/Ro (60 kDa, 52 kDa), SS-B/La, Centromere B, Scl-70, Jo-1, fibrillarin, RNA Pol III, Rib-P, PM-Scl, PCNA, Mi-2 proteins, Sm proteins and native purified DNA), EliA β2-Glycoprotein I IgG, EliA β2-Glycoprotein I IgM, EliA Cardiolipin IgG, EliA Cardiolipin IgM, EliA dsDNA, EliA Jo-1, EliA La, EliA Mi-2, EliA Ro52, EliA Ro60, EliA MPO^S, EliA PR3^S, EliA RNA Pol III, EliA Scl70^S and EliA RF IgM. Capillary serum sample volume was significantly smaller compared with the venous sample volume. In order to be able to screen the capillary serum samples for all 17 biomarkers despite the volume limitations, deviations from the manufacturer's instruction were made: After prediluting the samples manually instead of using the automated sample dilution performed directly by the instrument, the samples were screened for positive biomarkers in multiple runs on the Phadia 250 instrument. To minimise interassay variability, the biomarker-positive capillary serum samples that yielded enough volume for follow-up testing were prediluted manually again and remeasured in a single run on the high-throughput Phadia 2500 instrument. To analyse

operator-dependent variations due to manual dilutions, true duplicates in two separate tubes of the venous (reference) samples were included to the measurement.

Patient questionnaires

Patients completed a questionnaire including: level of agreement (1—totally disagree, 5—totally agree) to 'I would prefer to do blood draws at home independently instead of having to see someone for a venous blood collection' before and after first capillary blood self-collection and 'The instructions for blood collection were clear'. Perceived pain during venous and capillary blood collection was measured using a numerical pain rating scale (NRS; 0 no pain at all, 10 worst imaginable pain).[33] The 10-item System Usability Scale (SUS),[34] ranging between 0 (worst) and 100 (best), was used to assess perceived device usability. According to Bangor *et al*, a score >68 can be considered above average, >80 as high[34] and ≥85.5 as excellent.[35] The Net Promoter Score (NPS)[36] was used to assess acceptability, by asking how likely patients would recommend self-blood collection with the respective device to a friend or patient using an 11-point NRS (0—not at all likely to 10—extremely likely). Answers can then be categorised to three groups: detractors (0–6), passives (7–8), promoters (9–10). The final NPS is equal to the percentage of detractors minus the percentage of promoters. Furthermore, we asked patients what kind of instruction they preferred (paper/video/both) and if they believed that the quality of the capillary sample was sufficient for analysis (yes/no).

Statistical analysis

Demographics and questionnaire results were descriptively analysed. Results from the initial runs, where all three sample types for all 70 individuals were screened for all 17 biomarkers, were displayed in a concordance table, indicating if both the venous sample and the capillary sample classified the individual as positive or negative for each respective biomarker. The venous sample was considered to be the reference sample for each individual. Diagnostic accuracy was defined as the sum of the matched venous and capillary samples with concordant results, (eg, venous sample positive and capillary sample positive), divided by the total number of matched samples. Samples from biomarker-positive individuals were remeasured in one large run to minimise interassay variations. For the biomarkers with at least 10 positive individuals, group statistics were applied following the methodology presented by Nwankwo *et al*.[37] First, biomarker data were analysed for normal distribution using the Anderson-Darling goodness-of-fit test. Data following a normal distribution (Ro52) were analysed by paired t-test and Pearson correlation, whereas non-normally distributed data (CTD screen, PR3, RF IgM and CRP) were analysed using Wilcoxon rank test and Spearman's rank correlation. Bland-Altman graphs were used to visualise the per cent difference in biomarker results.

JMP software (V.15.0.0, SAS Institute) was used for the analysis.

RESULTS

Patient demographics

In total, 70 consecutive patients with IMRD were recruited between 17 May and 25 November 2021 (see table 1). Mean patient age was 54.9±12.4 years, 52 of 70 (74.3%) were female and 17 of 70 (11.4%) patients reported that they previously self-collected capillary blood. Most common main diagnosis was Sjogren's syndrome (n=19), followed by SLE (n=18), vasculitis (n=15), systemic sclerosis (n=5), myositis (n=5), antiphospholipid syndrome (n=3), mixed CTD (n=3) and RA (n=2). The majority of patients reported to be secondary school graduates (54 of 70; 77.1%).

Blood collection success rate

All patients, except for one patient using a Tasso+ device (69 of 70), were able to successfully collect capillary blood using an UA collection device. Despite correct usage of the Tasso+ device and heat pad, the patient could not collect any capillary blood. During the first supervised capillary blood collection, protocol deviations causing study personnel intervention were registered in 6 of 35 (17%) and 8 of 35 (22%) in the Tasso+ and TAP II group, respectively (online supplemental table 1). No protocol deviations that would have required intervention by the study personnel were registered during the second supervised capillary blood collection in the first part of the study. Online supplemental tables 2 and 3 list the percentage of correctly completed manual steps for the Tasso+ and TAP II device, respectively. Irrespective of the device and respective manual, most patients forgot to set a timer to track blood collection duration. One unsupervised (according to patient successfully collected) Tasso+ sample was lost during shipment. In summary, using the Tasso+ and TAP II, 28 of 35 (80.0%) and 27 of 35 (77.0%) were able to successfully and safely collect capillary blood within the first attempt. In a second attempt, all supervised patients (20 of 20) safely carried out the blood collection, and 34 of 35 (97.1%) and 35 of 35 (100.0%) successfully collected blood using Tasso+ and TAP II, respectively. Mean Tasso+ and TAP II serum volume was 287 µL (range 0–475 µL) and 233 µL (range 55–350 µL), respectively.

Agreement of capillary and venous blood results

We registered very high overall concordance between capillary and venous samples (94.7% and 99.5% for positive and negative samples, respectively) (see table 2). Variation was due to samples that were close to cut-off and would have been remeasured in clinical routine. Online supplemental tables 4 and 5 depict the similarly good concordance of the samples incubated for 72 hours and independently collected by patients, respectively. All autoantibody biomarkers showed high correlation (r or ρ) of ≥0.98 between capillary and venous samples

Table 1 Patient demographics and disease characteristics

Parameter	Total (n=70)	Tasso+ (n=35)	TAP II (n=35)
Age, years, mean±SD	54.9±12.4	53.5±12.2	56.3±12.6
Age, years, median (IQR range)	55 (25–80)	53 (25–75)	56 (26–80)
Female, n (%)	52 (74.3)	27 (77.1)	25 (71.4)
BMI, kg/m^2, mean±SD	27.1±6.1	28.2±6.3	26.1±5.7
Self-sampling experience, n (%)	17 (24.3)	11 (31.4)	6 (17.1)
Current smokers	8 (11.4)	3 (8.6)	5 (14.3)
Diagnosis, n (%)			
Systemic lupus erythematosus	18 (25.7)	10 (28.6)	8 (22.9)
Primary Sjogren's syndrome	19 (27.1)	8 (22.9)	11 (31.4)
Rheumatoid arthritis	2 (2.9)	1 (2.9)	1 (2.9)
Systemic vasculitis	15 (21.4)	7 (20.0)	8 (22.9)
Antiphospholipid syndrome	3 (43)	1 (2.9)	2 (5.7)
Myositis	5 (7.1)	3 (8.6)	2 (5.7)
Systemic sclerosis	5 (7.1)	2 (5.7)	3 (8.6)
Mixed connective tissue disease	3 (4.3)	3 (8.6)	0 (0.0)
Education status, n (%)			
Primary school graduate	4 (5.7)	2 (5.7)	2 (5.7)
Secondary school graduate	54 (77.1)	29 (82.9)	25 (71.4)
University graduate	12 (17.1)	4 (11.4)	8 (22.9)

BMI, body mass index.

(figure 3). For CTD screen, PR3 and Ro52, no significant difference between capillary and venous sample was observed, while borderline significance for RF IgM (p=0.0507) was found. For CRP, we observed a high correlation (Spearman r=0.5990, p=0.0396). For CTD screen, no significant difference was observed between self-sampling device types (online supplemental figure 1). For the biomarkers with less than 10 positive individuals, the difference in biomarker concentrations between the capillary sample and the venous sample was depicted in summary graphs (online supplemental figures 2–4). For the biomarkers CTD screen, RF IgM, PR3 and CRP, enough positive unsupervised at-home samples were collected by patients to perform statistical evaluation. Among them, no significant differences between unsupervised capillary samples and venous reference samples centrifuged at the draw date at the hospital were observed (online supplemental figure 5).

Patients' perception
Pain
Mean pain NRS (range 0–10) scores for capillary self-sampling were similar for both devices and lower compared with standard venous blood collection (Tasso+: 1.3±0.5 vs 2.9±2.0; TAP II: 1.4±0.7 vs 2.5±1.6), resulting in reduced pain compared with venous blood collection for the majority of patients (online supplemental figure 6).

Usability
Perceived usability was excellent and comparable for both devices with mean SUS scores of 88.6 and 86.0 for Tasso+ and TAP II, respectively (online supplemental table 6).

Acceptance
The proportion of promoters for Tasso+ was 19 of 35 (54.3%) vs 17 of 35 (48.6%) for TAP II, while 9 of 35 (25.7%) vs 7 of 35 (20.0%) were detractors, respectively, resulting in a positive NPS for both devices of +28.6% (online supplemental figure 6). Thirty-nine of 70 (55.7%) patients (Tasso+: 17 of 35 (48.6%); TAP II: 22 of 35 (62.9%)) agreed or strongly agreed to prefer self-collection over visiting a healthcare professional for a venous blood collection.

Instructions and sample quality
Sixty-three of 70 (90.0%) patients (Tasso+: 32 of 35 (91.4%); TAP II: 31 of 35 (88.6%)) agreed or strongly agreed that the available instructions were clear. The majority of patients (36 of 70 for both devices; Tasso+: 15 of 35 (42.9%); TAP II: 21 of 35 (60.0%)) would like to have access to video and written instructions compared with written instructions only (24 of 70 for both devices; Tasso+: 18 of 35 (51.4%); TAP II: 6 of 35 (17.1%)) and video instructions only (10 of 70 for both devices; Tasso+: 2 of 35 (5.7%); TAP II: 8 of 35 (22.9%)). The majority of patients assumed that the quality of the first capillary

Table 2 Concordance of venous and capillary blood measurements

Parameter	Concordance	
	Positive samples (capillary/venous)	Negative samples (capillary/venous)
CTD screen	97.7% (42/43)	100% (25/25)
dsDNA	100% (10/10)	96.4% (54/56)
RF IgM	93.8% (15/16)	100% (51/51)
PR3	92.3% (12/13)	100% (54/54)
MPO	100% (2/2)	100% (65/65)
SS-A/Ro52	100% (19/19)	100% (48/48)
SS-A/Ro60	100% (2/2)	100% (65/65)
SS-B/La	100% (11/11)	100% (56/56)
ß2-Glycoprotein I IgG	100% (5/5)	100% (61/61)
ß2-Glycoprotein I IgM	71.4% (5/7)	100% (61/61)
Cardiolipin IgG	100% (2/2)	100% (64/64)
Cardiolipin IgM	100% (1/1)	100% (65/65)
Mi-2	0% (0/1)	100% (65/65)
Jo-1	100% (2/2)	100% (64/64)
RNA Pol III	100% (2/2)	100% (65/65)
Scl-70	100% (2/2)	100% (65/65)
CRP	85.7% (12/14)	93.5% (43/46)

CRP, C reactive protein; CTD, connective tissue disease; dsDNA, double-stranded DNA; MPO, myeloperoxidase; PR3, proteinase 3; RF, rheumatoid factor.

sample was sufficient for laboratory analysis (Tasso+: 26 of 35 (74.3%); TAP II: 28 of 35 (80.0%)). The patient not being able to collect any capillary blood using the Tasso+ device correctly assumed that no laboratory analysis was possible.

DISCUSSION

To the best of our knowledge, this is the first capillary self-collection study investigating a broad variety of autoantibodies. Additionally, the success rate and usability of two UA-based devices have not been previously compared.

Our study showed that self-collection of capillary blood using UA-based devices is feasible by patients with IMRD with a similarly high success rate, usability and acceptance for both devices and reduced pain compared with venous blood collection. Importantly, the study also demonstrated excellent concordance of venous-based and capillary blood-based samples with high agreement of autoantibody levels, suggesting clinical interchangeability. Moreover, this study indicates that home sampling and conventional mail postage do not negatively affect sample quality for the autoantibody biomarkers evaluated in this study.

The high success rate of self-collection (all patients within two attempts) is in line with studies evaluating previous models of the UA-based devices, reporting failure rates of 6.6% (6 of 91),[26] 20% (6 of 30),[29] 2% (2 of 108)[27] and 4% (10 of 240).[38] Previous studies showed several limitations including: being not carried out manufacturer independent, devices not actually used independently by patients and no safety analysis. To our knowledge, no blood self-collection study has previously analysed correct execution of the manual instructions in such detail, providing in-depth information to guide successful and safe implementation. Importantly, without supervision and only guided by video and manual instructions, a substantial number of patients made mistakes. These results indicate that patients should have access to support at least for their first time using a self-collection device. Support could be either remotely via mail, chat, telephone, video consultation[39] or ideally in the form of physical assistance by a trained healthcare professional.

A major reason for a higher success rate of blood collection compared with our previous trial could be using chemical heat pads instead of hand rubbing. In the previous trial, patients often did not know how fast or hard to rub the skin to increase capillary blood flow and sometimes accidentally scratched themselves. Using heat pads is a more standardised way to increase vasodilation and improve the self-sampling success rate.

Measurement of autoantibodies is essential in the diagnosis and classification of rheumatic diseases.[3 4 40 41] Herein, we report very good concordance of capillary blood for a total of 16 autoantibodies. This interchangeability of capillary and venous blood is in line with recent anti-SARS-CoV-2 antibody investigations, reporting accuracy rates of 98.9%[26] and Cohen's kappa coefficient of >0.88[42] and 0.92.[43] All discordant values were due to close cut-off borderline values, which would have been retested in clinical routine.

We anticipate that self-sampling will initially be part of the secondary 'self-pay' healthcare market enabling a faster low-barrier remote diagnostic pathway.[44] Nearly half of all patients used an online search engine prior to their first rheumatology appointment.[12] As current symptom checkers are not very reliable,[14] self-sampling kits could be sent to patients to improve diagnostic accuracy in a second step. These results and any additional diagnostic procedures could be discussed virtually via
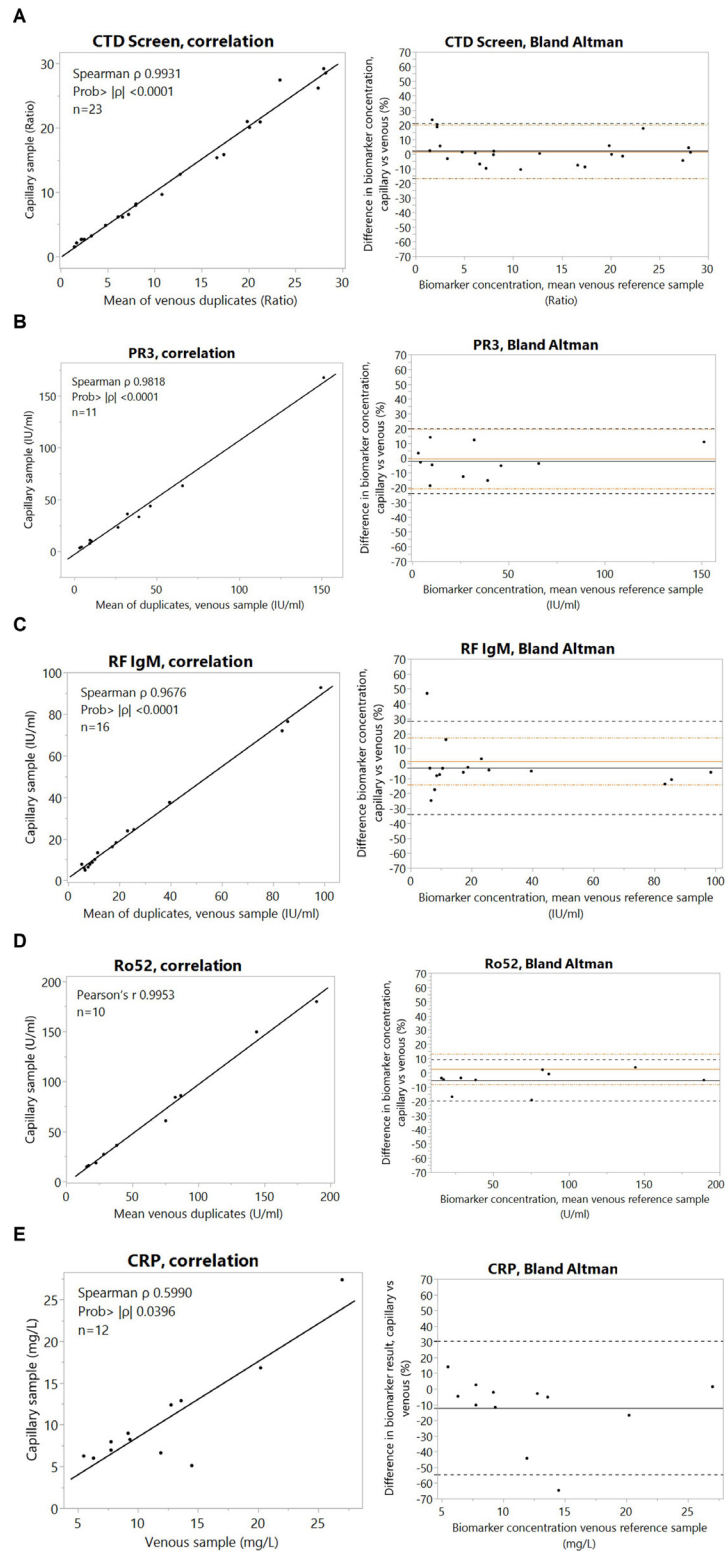
Figure 3 Correlation and agreement between capillary and venous blood results according to respective serological biomarker. Filled beige lines: mean of difference between venous duplicates; dashed beige lines: 95% CI (±1.96 SD). Filled black lines: mean of difference between capillary device sample and venous reference sample (mean of duplicates); dashed black lines: 95% CI. (A) CTD screen (n=23): Spearman's r=0.9931 p<0.0001; Wilcoxon p=0.7436, Bland-Altman: mean 2.2 (−16.6 to 21.0), venous mean: 1.6 (−16.6 to 19.9). (B) PR3 (n=11): Spearman's r=0.9818 p<0.0001; Wilcoxon p=0.7856, Bland-Altman: mean −2.03 (−23.8 to 19.8), venous mean: −0.63 (−20.7 to 19.5). (C) RF IgM (n=16): Spearman's r=0.9676 p<0.0001; Wilcoxon p=0.0507, Bland-Altman: mean −2.87 (−34.2 to 28.4), venous mean: 1.4 (−14.3 to 17.1). (D) Ro52 (n=10): Pearson's r=0.9928, paired t-test: p=0.1845, Bland-Altman: mean −5.32 (−19.8 to 9.2), venous mean: 2.42 (−8.4 to 17.1). (E) CRP (n=12): Spearman's r=0.5990 p=0.0396; Wilcoxon p=0.0449, Bland-Altman: mean −12.1 (−54.6 to 30.5). CRP, C reactive protein; CTD, connective tissue disease; PR3, proteinase 3; RF, rheumatoid factor.

video consultations. Based on the promising results of an online self-referral tool for patients at risk of axial spondyloarthritis,[45] we are currently investigating this tool combined with capillary remote self-collection for determination of CRP and HLA-B27 status.

Point-of-care tests with the advantage of immediate results are rarely needed, offering qualitative (positive/negative) results for selected biomarkers, with varying concordance[46] compared with laboratory-based testing: (anti-CCP2: sensitivity and specificity of 95%[47] to 100%[48]; anti-MCV[49]: sensitivity 69.3%, specificity 99.7%; RF IgG[49]: sensitivity 69.3%, specificity 99.7%).

Remote longitudinal serological monitoring could improve early flare detection,[25] reduce clinical visits,[50] offer time-saving for patients and clinicians, empower patients and improve shared decision-making.[37] It would add valuable objective data to complement currently available remote PROs, such as electronic questionnaires[51] and wearable data.[52] Exact quantification of autoantibody levels is currently not clinically relevant for all IMRDs, however, increasing evidence exists for MPO,[9] PR3[8 9] and especially dsDNA,[7] and our study demonstrates clinical utility with very good agreement for PR3 (r=0.9818 (p<0.0001), mean bias −2.03%). In agreement with previous studies,[26 37 53] we did not observe a clinically significant effect of delayed sample processing and uncontrolled conventional mail postage.

We are currently conducting a trial in patients with axial spondyloarthritis in disease remission using electronic questionnaires and the TAP II device to collect blood for an exact CRP quantification, allowing completely remote disease activity evaluation (ASDAS-CRP[6]). In order to provide completely remote care for patients in stable disease remission on immunosuppression, drug safety analysis via self-blood collection would also need to be assured. Mixed data exist on equivalence of capillary blood, regarding liver[37] and kidney function tests[37 54] and complete blood count.[37 55 56] Promising results have been recently published regarding completely non-invasive measurement of CRP via saliva[57] or even continuously real time via a sweat-based wrist wearable.[58]

In line with our results, previous studies could demonstrate that UA-based self-sampling is perceived as less painful compared with traditional venous blood collection[28] and finger pricking.[27] Similarly, perceived usability of both devices (SUS: Tasso+: 88.6; TAP II: 86.0) was higher compared with finger pricking (61.0[37] and 80.7[29]), likely due to automatic blood collection. The NPS (likelihood to promote device) of both devices was as high (+28.6%) as in our previous study, comparing a former Tasso version with finger pricking (Tasso-SST: NPS +28%; finger pricking −20%).[29] The advantages of UA devices are accompanied by higher costs compared with conventional FP devices. To ensure correct device usage, provision of written instructions and video instructions seems advisable according to our study and a previous implementation study.[37]

This pilot study has several limitations, including the limited size and cross-sectional nature. For some biomarkers, such as CRP and dsDNA, only a small number of positive values was available. Additionally, we did not specifically investigate potential adverse events. Furthermore, two sample labelling errors occurred in this study indicating that institutions that aim to implement home-sampled specimen processing should emphasise the importance of a standardised sampling and labelling workflow.

Our study provides promising real-world and manufacturer-independent evidence. Manufacturers were not involved in the design or deployment of the study except for provision of the respective devices. Importantly, the study was designed in collaboration with designated patient research partners and we were able to include a diverse group of patients, including patients with different rare diseases. Translating our results into clinical routine, we are currently conducting several prospective longitudinal trials to explore new clinical pathways including self-sampling.

CONCLUSION

Collection of capillary blood via UA-based devices can reliably be carried out by patients with CTDs and is well accepted. The excellent concordance between capillary and venous blood collection highlights the potential of this technology to complement rheumatology care and research.

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