

'good', 'moderate', 'none') after surgical completion, drug consumption, inhibitor development and the number of days in hospital were analysed.

**Results:** Interim analysis included 45 major surgeries in 33 patients, of which 27 surgeries were new, previously unreported cases. The 45 major surgeries included 21 prosthesis related (10 of which were joint replacements), 11 synovectomy and/or debridement procedures, six arthrodesis and seven other procedures. Among the 41 orthopaedic procedures, two were emergencies and the remaining 39 were elective. Haemostasis was successful (those rated 'excellent' or 'good') in 39/41 (95.1%) orthopaedic surgeries (two had 'moderate' haemostatic response) and 43/45 (95.6%) major surgeries. The overall N8-GP dose range was 27.2-136.2 IU/kg, and the number of N8-GP doses was one to three. Four bleeds (all in joints) were reported in post-operative Days 1-14, of which three were successfully treated. Only one patient required an additional intra-operative dose of N8-GP (20.7 IU/kg). N8-GP did not show any safety concerns or indication of inhibitor development. The number of hospital days ranged from zero to 39 days.

**Relevance:** N8-GP can be successfully used for the peri-operative management of elective and emergency orthopaedic surgery in patients with severe haemophilia A.

## A pilot study on effectiveness of aquatic therapy with Ai Chi techniques for arthritic knee joint in haemophilia patients

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**Introduction and Objective:** Due to the lack of appropriate factor supply, joints bleeds are treated with on demand factor therapy or PRICE protocol which leads to joint arthropathy causing disability, which results in poor Quality of Life. Aim of the study is to provide an appropriate treatment programme for joint arthropathy in a low cost and effective manner. Aquatic therapy refers to treatments and exercises performed in water for relaxation, fitness, physical rehabilitation. Ai-chi is a total body relaxation and strengthening progression used for aquatic therapy; this is characterized by slow movement coordinated with deep breathing, based on elements of tai-chi.

**Materials and Methods:** 15 subjects were included in this pilot study obtaining informed consent. The stretching and strengthening exercise using noodles, dumbbells etc is followed by 12 basic movements of ai-chi. Sessions continued for 60-90 minutes 6 days/week for a period of 45 days. Pre- and post-assessment were done. The assessment tools include HJHS, ROM, MMT, VAS, 6MWT, quality of life S F 36 and FISH.

**Results:** The changes observed in the tools such as HJHS (36.67 + 12.181 vs 27.20 + 11.390,  $P = 0.001$ ), FISH (21.93 + 3.788

vs 24.67 + 3.754,  $P = 0.003$ ), Flexion ROM (95.5 + 24.577 vs 100.83 + 23.083,  $P = 0.030$ ), Extension ROM (14.57 + 12.153 vs 9.23 + 10.301,  $P = .000$ ) Flexion MMT (3.00 + 0.000 vs 4.00 + 0.000,  $P = .000$ ), Extension MMT (3.00 + 0.000 vs 4.00 + 0.000,  $P = 0.000$ ), SPO2 (98.2667%+ .79881% vs 98.7333%+ .59362%,  $P = 0.035$ ), Distance Travel (125.27 + 17.219 vs 156.80 + 26.320,  $P = 0.001$ ), BORG (1.87 + 1.807 vs .53 + .834,  $P = 0.027$ ), and QOL SF 36 (88.66667 + 4.8648 vs 95.06667 + 3.261,  $P = 0.000$ ) were also highly significant.

**Conclusion:** There is an improvement in all the variables. Concentration power, gait pattern, posture and ability to control emotions have been increased. Therapy helps to improve the joint status as well as overall health without much strain.

## DNA and neutrophil extracellular traps release, novel potential biomarkers and therapeutic targets of joint Damage In Hemophilia

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**Background and aim:** Hemarthroses cause major morbidity in hemophilia resulting in chronic hemophilic synovitis (CHS), osteochondral degeneration and arthropathy. Although the initial events causing joint damage remain uncertain, iron and monocytes-induced inflammation are known players in this process. The role of neutrophils, major immune blood cells infiltrated in synovium after bleeding is unknown. Neutrophils release extracellular DNA traps (NETs), microbicidal structures containing DNA fibers with bound granular enzymes as elastase. During chronic inflammation, a cytotoxic effect of NETs has been associated with tissue damage in lung, kidney, skin and joints. Our aim is to elucidate the role of neutrophils in CHS by studying the formation of synovial NETs and its correlation with joint damage.

**Methods:** Synovial fluids (SF) and peripheral blood-derived plasma were obtained from 16 patients (29 ± 11 years old, 15 Haemophilia type A, 1 type B). Chronic synovitis was present in 1 ankle and 16 knee joints that were evaluated for Haemophilia Joint Health Score (HJHS). NETs in SF and plasma were indirectly determined by quantification of DNA (fluorometry) and directly by measuring DNA-Elastase complexes (ELISA). Pearson or Spearman correlations with clinical parameters were calculated.

**Results:** DNA (0.39 ± 0.09 µg/mL) and DNA-Elastase (0.25 ± 0.03 Abs) were detected in SF of CHS patients and they were positively correlated with HJHS,  $r > 0.5$ ,  $p < 0.05$ . Moreover, incubation of SF with fresh blood-isolated neutrophils resulted in the release of NETs in vitro indicating that pro-NETotic factors remain active in SF. While DNA or DNA-Elastase were

not detected in plasma of healthy donors, they were found in the plasma of CHS patients (DNA =  $0.16 \pm 0.04$   $\mu\text{g}/\text{mL}$ ; DNA-Elastase =  $0.17 \pm 0.05$  Abs) and showed a strong positive correlation ( $r = 0.7$ ,  $P > 0.05$ ) with the synovial levels of both parameters.

**Conclusions:** Our data demonstrate that NETs are formed in synovium of CHS patients. The positive correlation of synovial DNA and DNA-Elastase levels with joint damage suggests that synovial NETs formation might be a potential therapeutic target for CHS. Moreover, the strong correlation of synovial and plasma levels of NETs suggests that circulating NETs represents a potential biomarker of CHS evolution.

## Elective orthopaedic surgery 'Excellence' Training Programme: Survey of past participants on the impact of multidisciplinary training

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**Introduction and Objectives:** Elective orthopaedic surgery (EOS) can positively impact quality of life for people with haemophilia (PwH), and an integrated multidisciplinary team approach is recommended. Potential lack of experience, low numbers of procedures and high perioperative complexity can make EOS interventions in PwH challenging. The EOS 'Excellence' Training Programme (EOS ETP) provides training for multidisciplinary teams to manage EOS in PwH. Overseen by a multidisciplinary Steering Committee, the 3-day programmes are hosted annually at established international centres of excellence; the core curriculum includes live surgery and case discussions. Since 2009, 13 programmes held at four centres were attended by 119 participants (surgeons, haematologists, physiotherapists) representing 33 countries; alumni meetings support ongoing best practice sharing. After a decade of the programme, the impact of the training on patient management was evaluated in a survey of previous participants.

**Materials and Methods:** A qualitative online survey was developed, approved by the Steering Committee and sent to previous EOS ETP participants to assess the effectiveness of the programme on 'strengthened confidence', 'patient care and/or surgical outcomes', and 'multidisciplinary team approach', among other aspects.

**Results:** Twenty-two past participants from 16 countries completed the survey (14 surgeons, 7 haematologists, 1 physiotherapist). Respondents entered the training having performed on average 13.4 (SD  $\pm$  23.14) surgical procedures in PwH (median 3.5; interquartile range [IQR] 1.25-16.5). Post-programme (median 4 years

since attendance), respondents reported performing an average of  $14.5 \pm 17.89$  interventions (median 7.0 [IQR 1-16]). Although analysis is limited by the small sample, numbers of surgical interventions were similar pre- and post-programme, and respondents consistently reported an increased confidence to manage surgery in PwH (100.0%) and in overall ability to refer PwH for surgery (90.9%) following the EOS ETP. Improved patient care and/or surgical outcomes as a result of the training were indicated by 81.8% of respondents, with the majority also reporting improvements in their multidisciplinary team approach (95.5%).

**Conclusions:** Surveyed EOS programme participants reported that the EOS ETP was an effective international training programme that enhanced multidisciplinary collaboration, strengthened confidence in managing surgical interventions in vulnerable populations, and improved overall patient care in their respective centres.

## The impact of progressive resistance training on physical function and quality of life in patients with haemophilia

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**Objective:** To evaluate the effects of a progressive resistance training program on physical function and quality of life in patients with haemophilia.

**Methods:** 20 patients (17 severe; 1 moderate; 2 mild) participated in the study. Patients were allocated to either an intervention group (strength training) or control (usual daily activities). The intervention group completed a training program for 2 days per week during 8 weeks. Sessions were performed 1-24 hours after prophylactic treatment and separated by 72 hours. The program consisted of the following exercises, performed with elastic bands: knee flexion, knee extension, ankle plantar flexion, ankle dorsal flexion, elbow flexion, elbow extension, shoulder abduction and hip abduction. In each session, the exercises were performed in a different order and in a rotation manner. Participants performed 3 sets of each exercise with 1-minute rest between sets and exercises. Intensity started with 20 repetition maximum (RM), and progressively increased each two weeks (i.e., 15RM, 12RM and finally 10RM). Patient global impression of pain change, isometric elbow extension/flexion strength, isometric knee extension/flexion strength, isometric ankle plantar flexion/dorsiflexion, quality of life (A36 Hemofilia-QoL<sup>®</sup>), the timed up and go test (TUG) and the sit-to-stand test were assessed.