ORIGINAL ARTICLE

The Effect of Trans-urethral Resection of the Bladder Tumour (TURBT) on Routine Haematological and Biochemical Blood Tests: A Clinical-pilot Observational Study

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ABSTRACT

Background: Bladder Cancer remains a major health burden, with over 10,000 new cases diagnosed annually in the UK. Around 80% of all cases are diagnosed as Non-Muscle Invasive Bladder Cancer (NMIBC), and 75% of patients have cancer recurrence and progression within 10 years. Patients with NMIBC are treated by Trans-Urethral Resection of the Bladder Tumour (TURBT), with approximately 8% of patients subsequently developing post-operative complications, such as bleeding, pain and infection. Currently, there is limited literature on the 'normal' pathophysiological response to TURBT for NMIBC, and predictors for post-operative complications. The aim of this clinical-pilot observational study was to evaluate changes in routine blood tests following TURBT. The objectives were to identify the 'normal' pathophysiological response after TURBT.

Methods: 34 consecutive patients aged between 57–94 years (median age: 72), scheduled for TURBT were recruited after written informed consent. Venous blood samples were collected from patients pre operatively (baseline), and post operatively at the following time points; 30 minutes, 120 minutes and 240 minutes post-operatively.

Results: Following TURBT, significant decreases were seen in several haematological and biochemical markers: haemoglobin ($p<0.01$), platelets ($p<0.01$), erythrocytes ($p<0.01$), haematocrit ($p<0.01$), plasma viscosity ($p=0.002$) activated partial thromboplastin time ($p= 0.004$), fibrinogen ($p<0.01$), potassium ($p<0.01$), globulin ($p=0.047$), alkaline phosphatase ($p=0.001$), and urea ($p=0.001$).

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Furthermore, significant increases were observed in numerous haematological and biochemical parameters: leukocytes (p=0.049), neutrophil count (p=0.022), prothrombin (p=0.014), bilirubin (p= 0.004), and alanine transaminase (p=0.004).

Conclusion: Significant changes to several routine blood tests occur following TURBT, and in general, it appeared that the most noticeable changes occurred between 30 and 120 minutes post-operatively. This clinical-pilot study may therefore provide a sound platform to undertake larger studies, to fully establish the effect of TURBT on routine blood tests, and could ultimately provide valuable information for doctors that may help with the clinical management of patients. (*Int J Biomed Sci* 2020; 16 (4): 68-74)

Keywords: Bladder Cancer; Trans-urethral Resection of the bladder Tumour (TURBT); Urology; Post-operative complications; Surgery; Blood tests

BACKGROUND

Bladder Cancer (BC) is one of the top ten most common cancers, which affects over 10,000 people in the UK annually. BC incidence is higher in men compared to women, presenting a 3:1 ratio (1, 2). Over 75% of BC cases appear in the superficial layer as Non-Muscle Invasive Bladder Cancer (NMIBC), and presents with high recurrence (60%) and Progression Rates (20%) within 10 years (3). Specifically, NMIBC is a papillary tumour, which starts to invade the lamina propria or the sub-epithelial connective tissue.

Currently, the European Association of Urology (EAU) guidelines indicate that patients who are suspected of having bladder cancer, must undergo Trans-Urethral Resection of the Bladder Tumour (TURBT) surgery, as a diagnosis for bladder cancer and subsequently a treatment for NMIBC.

In 2011, 11% of TURBTs were performed as day case surgeries, whereas in 2014, a significant increase (68%) were performed as day case surgeries (4). Complication rates following TURBT surgeries has been reported at 8%, with bladder perforation, pain, infection and bleeding being the most common complications (5, 6). With an ageing population, increase in incidence rates and high recurrence rates, it is anticipated that the number of TURBT will increase, and consequently will lead to an increase in post-operative complications, which can be appreciated to involve patients requiring longer hospital stays, poor patient experience and outcomes, and additional financial constraints for the NHS.

Whilst we, and others, have previously reported post-operative changes in routine blood tests following various surgical procedures (7-13-17), crucially, there is very little evidence investigating the direct effect of TURBT, for diagnosis of NMIBC on routine blood tests. Specifically, Hughes *et al*., [2013] have reported that lower limb orthopaedic surgery results in changes to coagulation (e.g. D-dimer) and non-specific inflammatory (e.g. CRP) biomarkers. During this study the most noticeable changes in biomarker levels occurred during days 1 to 3 postoperatively, with these changes being suggested to influence postoperative clinical outcomes such as oedema, pyrexia and pain.

With respect to urological procedures, Moyes *et al*., [2017] have reported significant changes in haematology (i.e. red blood cells, white blood cells, neutrophils, and platelet counts) and biochemistry (i.e. CRP, total protein, bilirubin, alkaline phosphatase, sodium and potassium) parameters following Flexible Ureterorenoscopy (FURS), for the treatment of kidney stones. During this study, it was concluded that some of the significant data presented may represent the 'normal' post-operative response following FURS, as no major complications occurred in most patients recruited in the study.

More recently, Hughes *et al*., [2020] have reported on changes to routine blood tests following shock wave lithotripsy (SWL), for the treatment of small kidney stones. Interestingly, the changes seen during this study followed a similar pattern to those reported by Moyes *et al*., [2017]. We therefore believe that by evaluating the role of routine blood tests following TURBT would provide a welcomed addition to the urological literature, to further help our understanding of the post-operative course following routine urological surgical procedures.

The aim of this observational study was to evaluate changes to routine blood tests (haematology and biochemistry) following TURBT. It was our expectation to enhance the current urological literature, by adding evidence-based

insight on this topic, where the results may help to identify the 'normal pathophysiological' response for patients undergoing TURBT. Ultimately, this could help predict those at increased risk of developing post-operative complications. Subsequently, this observational study would form a sound basis to undertake future investigations employing a larger cohort, involving multi-centre institutions.

METHODS

Subject Volunteers and TURBT

Ethical approval for this observational study was received from the Welsh Research Ethics Service 4 Committee (REC4:14/WA/0033), UK. Thirty-four consecutive patients who underwent TURBT surgery, for the diagnosis of NMIBC were recruited after written informed consent (n=34). The patients, 28 Males and 6 Females (ratio 4.7:1), were aged between 57-94 years (median age: 72). Treatment was given as per standardised protocol in our institution, using the Olympus system 400 resectoscope and TURIS bioplar diathermy, whilst under general or spinal anaesthesia.

Blood Samples

Venous blood samples were collected from patients via the ante-cubital fossa pre-operatively on the morning of the procedure, which stood as a control (baseline) measurement. Following TURBT, subsequent blood samples were collected at 30 minutes, 120 minutes and 240 minutes post-operatively. Three vacutainers of blood were collected, namely di-potassium ethylene diamine tetraaceticacid (EDTA), tri-sodium citrate and serum separator tube. All routine haematological and biochemical parameters were analysed, at the Betsi Cadwaladr University Health Board (BCUHB) Pathology Laboratory, Wrexham Maelor Hospital, North Wales (UK), using fresh whole blood, plasma or serum samples.

Measurement of full blood counts

Full blood counts was performed using a Sysmex XE-5000 automated cell counter using blood collected in EDTA tubes.

Measurement of haemostatic function

Tri-sodium citrated blood samples were used to measure haemostatic function, namely activated partial thromboplastin time (aPTT) (seconds), Prothrombin Time (PT) (seconds) and Fibrinogen (g/L). All tests were undertaken employing a Sysmex CS2100 analyser.

Measurement of plasma viscosity (PV)

Plasma viscosity (mPa/second) was measured using a Benson BV200 Viscometer, from blood collected in EDTA tubes.

Measurement of biochemistry parameters

Biochemistry parameters were measured using blood collected in serum separator tubes, employing the Beckman Coulter AU5800 and AU680 analysers.

Statistical analysis

Results were presented as mean ± standard error (SE) or median ± minimum/maximum. Where data was normally distributed repeated measure one-way analysis of variance (ANOVA) between sample tests was employed, adopting a 5% level of significance. Post hoc testing was conducted using the Bonferroni test for pairwise comparisons between means. Data that did not comply with normality were analysed using the Friedman test. Where the Friedman test resulted in statistical significance, subsequent tests were performed using the Wilcoxon tests. Statistical significance was accepted when $p \leq 0.05$.

RESULTS

Haematological Blood Results

Table 1 illustrates the changes observed in haematological parameters following TURBT, for the diagnosis and subsequent treatment of bladder cancer (n=34). Significant decreases were observed post-operatively in the following parameters: haemoglobin ($p<0.01$), platelets ($p<0.01$), erythrocytes ($p<0.01$), haematocrit ($p<0.01$), plasma viscosity ($p= 0.002$) activated partial thromboplastin time ($p= 0.004$), and fibrinogen ($p<0.01$). Significant increases can be seen in the following haematological parameters, leukocytes ($p=0.049$), neutrophil count ($p=0.022$), and prothrombin ($p=0.014$).

Biochemical Blood Results

Table 2 illustrates the changes observed in biochemical parameters following TURBT, for the diagnosis and subsequent treatment of bladder cancer (n=34). Significant decreases were observed within biochemical parameters post-operatively: potassium ($p<0.01$), globulin ($p=0.047$), alkaline phosphatase ($p=0.001$), and urea ($p=0.001$). Significant increases were observed in the following biochemical parameters: bilirubin ($p=0.004$), and alanine transaminase ($p=0.004$).

Table 1. The effect of TURBT on haematological parameters (n=34)

Haematological Parameters	Baseline	30 Minutes	120 Minutes
Leukocytes (× 10^9/L)	8.05 (± 4.2/16.8)	6.85 (± 4.9/13.4) *	8.1 (±5.50/15.30)
Haemoglobin (g/L)	146.50(± 96/181)	131.50 (± 95/149) *	136.0 (± 86/169)*
Platelets (× 10^9/L)	240.5 (±148/527)	220.0 (±124/412) *	226.0 (± 143/433)*
Erythrocytes (× 10^9/L)	4.74 (±3.05/6.01)	4.32 (±3.20/4.95)*	4.39 (± 2.77/5.89)*
Haematocrit	0.44 (±0.29/0.52)	0.40 (±0.30/0.44)*	0.40 (± 0.26/0.51)*
Mean Cell Volume (MCV) (fl)	91.61 ± 0.72	92.15 ± 0.79	91.60 ± 0.69
Mean Cell Haemoglobin (MCH) (pg)	30.20 (±28.70/34.70)	29.90 (± 28.90/33.90)*	30.15 (±28.30/34)
Neutrophil Count (× 10^9/L)	5.4 (± 2.30/14.70)	4.65 (± 3.00/12.20)*	5.9 (± 3.20/13.50)
Lymphocyte Count (× 10^9/L)	1.65 ± 0.09	1.52 ± 0.09	1.47 ± 0.09
Monocyte Count (× 10^9/L)	0.65 (± 0.20/1.50)	0.60 (± 0.10/0.90)	0.70 (± 0.10/1.10)
Eosinophil Count (× 10^9/L)	0.10 (±0.0/0.70)	0.10 (± 0.0/0.90)	0.10 (± 0.0/0.90)
Basophil Count (× 10^9/L)	0.00 (± 0.0/0.20)	0.00 (± 0.0/0.10)	0.00 (±0/0.20)
Plasma Viscosity (mPa)	1.67 (±1.44/2.03)	1.53 (±1.38/1.72)*	1.59 (± 1.39/1.81)*
PT (Seconds)	11.05 (± 10.10/13.40)	11.60 (±10.80/30.50)*	11.30 (±10.60/12.80)*
APTT (Seconds)	26.66 ± 0.55	25.98 ± 0.53	25.87 ± 0.45*
Fibrinogen (g/L)	3.55 (± 1.90/7.80)	3.10 (± 1.50/6.10)*	3.40 (± 1.70/6.50)*

Haematological Parameters	240 Minutes	Trend	P Value	Statistical tests
Leukocytes (× 10^9/L)	8.9 (±5.50/13.60)	↑	P= 0.049	Friedman + Wilcoxon
Haemoglobin (g/L)	133.5 (± 120/156)*	↓	P<0.01	Friedman + Wilcoxon
Platelets (× 10^9/L)	226.0 (± 140/336)*	↓	P<0.01	Friedman + Wilcoxon
Erythrocytes (× 10^9/L)	4.45 (± 3.96/5.07)*	↓	P<0.01	Friedman + Wilcoxon
Haematocrit	0.41 (±0.37/0.46)*	↓	P<0.01	Friedman + Wilcoxon
Mean Cell Volume (MCV) (fl)	91.21 ± 0.83	↓	P=0.102	ANOVA
Mean Cell Haemoglobin (MCH) (pg)	30.28 (± 28.60/33.80)*	↓	P=0.012	Friedman + Wilcoxon
Neutrophil Count (× 10^9/L)	6.15 (± 3.20/12.50)	↑	P=0.022	Friedman + Wilcoxon
Lymphocyte Count (× 10^9/L)	1.51 ± 0.14	↓	P=0.131	ANOVA
Monocyte Count (× 10^9/L)	0.55 (± 0.10/1.20)	↓	P=0.430	Friedman
Eosinophil Count (× 10^9/L)	0.15 (± 0/0.90)	↑	P=0.702	Friedman
Basophil Count (× 10^9/L)	0.00 (± 0.0/0.10)	-	P=0.733	Friedman
Plasma Viscosity (mPa)	1.53 (± 1.41/1.72)*	↓	P=0.002	Friedman + Wilcoxon
PT (Seconds)	11.73 (± 10.80/14.30)	↑	P=0.014	Friedman + Wilcoxon
APTT (Seconds)	25.55 ± 0.68	↓	P=0.004	ANOVA + Bonferroni
Fibrinogen (g/L)	3.10 (±1.60/4.70)*	↓	P<0.01	Friedman + Wilcoxon

Data analysed via Friedman testing was presented as median ± minimum/maximum, whereas data analysed via ANOVA is presented as means ± standard error. Statistical significance following post-hoc analysis was represented when *$p \leq 0.05$.

Table 2. The effect of TURBT on biochemical parameters (n=34)

Biochemistry	Baseline	30 Minutes	120 Minutes
Sodium (mmol/L)	138 (± 127/142)	138 (± 132/142)	137 (± 130/141)
Potassium (mmol/L)	4.5 (± 3.60/6.70)	4.5 (± 3.80/5.50)	4.4 (± 3.80/5.70)
Creatinine (µmol/L)	78 (± 59/257)	75 (± 5.90/119)	76 (± 6/254)
Estimated GFR (ml/min/1.73m^2)	79 (± 21/90)	84 (± 51/90)	77 (± 21/90)
C-Reactive Protein (mg/L)	3.0 (± 1/126)	4.0 (± 1/119)	3.0 (± 1/125)
Bilirubin (µmol/L)	9 (± 5/18)	9 (± 5/22) *	10 (± 5/23) *
Total Protein (g/L)	70.31 ± 0.82	60.86 ± 1.16	63.96 ± 0.73
Albumin (g/L)	41.34 ± 0.53	35.95 ± 0.70	37.83 ± 0.53
Globulin (g/L)	29 (± 20/40)	25 (± 18/33) *	26 (± 18/35)*
Alkaline Phosphate (U/L)	80 (± 51/149)	73 (± 43/118) *	77 (± 47/130)
Alanine Transaminase (U/L)	20 (± 7/51)	17 (± 9/83)*	17 (± 8/47)*
Urea (mmol/L)	5.9 (± 4/20.10)	5.2 (± 3.60/8.60) *	5.4 (± 3.50/19.80)*

Biochemistry	240 Minutes	Trend	P Value	Statistical Tests
Sodium (mmol/L)	138 (± 136/143)	↑	P=0.740	Friedman
Potassium (mmol/L)	4.1 (± 3.50/4.80)	↓	P<0.01	Friedman + Wilcoxon
Creatinine (µmol/L)	79 (± 58/121)	↑	P=0.267	Friedman
Estimated GFR (ml/min/1.73m^2)	80.50 (±50/90)	↑	P=0.158	Friedman
C-Reactive Protein (mg/L)	5.0 (± 1/22)	↑	P=0.269	Friedman
Bilirubin (µmol/L)	10 (± 5/20) *	↑	P=0.004	Friedman + Wilcoxon
Total Protein (g/L)	63.16 ± 1.39	↓	P=0.093	ANOVA
Albumin (g/L)	36.5 ± 0.69	↓	P=0.058	ANOVA
Globulin (g/L)	26.50 (± 21/34)*	↓	P<0.01	Friedman
Alkaline Phosphate (U/L)	69.50 (± 48/106)	↓	P=0.001	Friedman + Wilcoxon
Alanine Transaminase (U/L)	17 (± 7/38)	↓	P=0.004	Friedman + Wilcoxon
Urea (mmol/L)	5.6 (± 3.7/9.0) *	↓	P=0.001	Friedman + Wilcoxon

Data analysed via Friedman testing was presented as median ± minimum/maximum, whereas data analysed via ANOVA is presented as means ± standard error. Statistical significance following post-hoc analysis was represented when *p≤0.05.

DISCUSSION

The aim of this clinical-pilot observational study was to investigate changes to routine haematological and biochemical parameters in patients following TURBT surgery. It was anticipated that the information gathered from this study, may help identify a 'normal' pathophysiological response to TURBT, and may ultimately help predict those patients at increased risk of developing post-operative complications, such as bleeding, pain and infection.

Bleeding is a common feature following TURBT, with haematuria being the most obvious manifestation. Although no complications developed in any of the patients recruited in our study, we report that significant changes to several parameters pertaining to the haemostatic process, including PT, fibrinogen, platelet and haemoglobin, occur following TURBT, which are indicative markers of bleeding. Our results compliment the work undertaken by Hughes *et al* [2013], which demonstrated an initial decrease in platelet counts and an increase in leucocyte counts, up

to 1-3 days post lower limb orthopaedic surgeries (10). Similar changes of decreasing platelet and increasing leucocyte counts were reported following TURBT. However, the study undertaken by Hughes *et al*., [2013], also investigated several other leukocytes, inflammatory and endothelial markers, which were not measured during the present study, mainly due to financial restrictions in being able to buy the necessary assay kits. Measuring these additional biomarkers such as CD11b, leukocyte elastase, protein C and vWF would have provided more information and contributed further to our understanding of the post-operative course following TURBT.

Specifically, following TURBT, changes to selective biological markers, such as total protein, albumin, alkaline phosphatase, bilirubin, total leukocytes, neutrophils, haemoglobin, erythrocytes, fibrinogen, and plasma viscosity were reported. Our group, BCUHB North Wales Clinical Research Centre (UK), have recently reported of similar changes to several routine blood parameters following shock wave lithotripsy (SWL) and flexible ureterorenoscopy (FURS), for the treatment of kidney stones (13, 14, 16, 17). Collectively, these changes in various blood parameters may therefore play an intrinsic role toward the 'normal' response following routine urological procedures. To date, the number of studies reporting on the effect of TURBT on routine blood parameters is limited, and therefore our contribution provides a welcome addition to the literature.

None of the patients involved during this study developed an infection or any other complications. A possible explanation for this could be that the urological surgeons involved in the study (and as part of current standard practice at our institution), administered antibiotics (Gentamicin) to all patients pre- and post-surgery, to minimize any risk of infection, and the potential of developing post-operative sepsis (a systemic response to infection). Although none of the patients undergoing TURBT in our study developed an infection, it may be appreciated that with the increased number of procedures undertaken on annual basis, the risk of developing post-operative infections following TURBT will increase and pose a problem for the management of these patients.

Collectively, the data from our study have shown that changes to several routine biochemical and haematological parameters, such as bilirubin, fibrinogen, and platelets, occur following TURBT, with the most noticeable changes occurring during 30 and 120 minutes post-operatively for most biomarkers. If these results are reproduced in larger studies, there is a putative suggestion that these markers may provide a more clinically relevant assessment of the extent of potential complications, such as bleeding that can occur following TURBT. However, it may be proposed that changes in the measured parameters during this study may not be due to a single factor, but due to multiple factors, such as the effects of anaesthesia, tissue damage and wound repair. However, to fully understand the effects of these multiple factors, further studies would need to be undertaken to directly investigate the effects of anaesthesia, tissue damage and wound repair on the measured parameters. However, undertaking such specific and additional investigations was beyond the scope and ethical limits of the present study, but no doubt provides a sound future direction to continue work in this area.

The main constraint of undertaking this observational clinical pilot-study was the relatively small number of patients recruited (n=34). However, the study does provide a sound platform for undertaking future work, which could be expanded to investigate the effect of TURBT on novel blood markers and their association with clinical outcome, and to have longer follow-up measurements (e.g. 12-72 hours post-operatively), involving larger cohorts and multi-centres.

It would also be interesting to recruit patients undergoing similar procedures, to provide an alternative control measure to that of using the patients themselves. In the present study we recruited patients who underwent general or spinal anaesthesia; a potential direction for future studies could compare the effects of these anaesthetic agents on some of the blood biomarkers that have been investigated in the study.

CONCLUSION

Significant changes to several routine blood tests occur following TURBT, and in general, it appeared that the most noticeable changes occurred between 30 and 120 minutes post-operatively. This clinical-pilot study may therefore provide a sound platform to undertake larger studies, to fully establish the effect of TURBT on routine blood tests, and could ultimately provide valuable information for doctors that may help with the clinical management of patients.

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CONFLICT OF INTEREST

The authors declare that no conflicting interests exist.

AUTHOR CONTRIBUTIONS

Conceived and designed the experiments: SFH, IS. Performed the experiments: RL, PET, AM, MI, SFH. Analysed the data: RL, MI, AD, SFH, IS. Contributed reagents/materials/analysis tools: SFH, IS. Wrote the paper: SFH, RL, AD, IS.

REFERENCES

1. Torre LA, Bray F, Siegel RL, Ferlay J, *et al*. Global Cancer Statistics. *CA: A Cancer Journal for Clinicians*. 2012. DOI: 10.3322/caac.21262.
2. Cancer Research UK. Bladder Cancer, Risks and Causes. http://www.cancerresearchuk.org/about-cancer/bladder-cancer/risks-causes. 2015.
3. Burger M, Catto JW, Dalbagni G, Grossman HB, *et al*. Epidemiology and Risk Factors of Urothelial Bladder Cancer. *European Association of Urology*. 2013; 63 (2): 234-241. DOI http://dx.doi.org/10.1016/j.eururo.2012.07.033.
4. Wells H. Day case TURBT: the new UK gold standard? *BAUS ePoster online library*. 2015; p99002.
5. Traxer O, Pasqui F, Gattegno B, Pearle MS. Technique and complications of transurethral surgery for bladder tumours. *British Journal of Urology International*. 2004; 94 (4): 492-496.
6. Gregg JR, McCormick B, Wang L, Cohen P, *et al*. Short term complication from transurethral resection of bladder tumor. *The Canadian Journal of Urology*. 2016; 23 (2): 8198-8203.
7. Beal AL, Scheltema KE, Beilman GJ, Deuser WE. Hypokalemia following trauma. *Shock*. 2002; 18: 107–110.
8. Hughes SF, Hendricks BD, Edwards DR, Middleton JF. Tourniquet-applied upper limb orthopaedic surgery results in increased inflammation and changes to leukocyte, coagulation & endothelial markers. PLOS ONE. 2010; 5(7): e11846. doi:10.1371/journal.pone.0011846.
9. Reissfelder C, Rahbari NN, Koch M, Kofler B, *et al*. Postoperative course and clinical significance of biochemical blood tests following hepatic resection. *British Journal of Surgery*. 2011; 98 (6): 836-844. DOI: 10.1002/bjs.7459.
10. Hughes SF, Hendricks BD, Edwards DR, Bastawrous SS, *et al*. Lower limb orthopaedic surgery results in changes to coagulation and non-specific inflammatory biomarkers, including selective clinical outcome measures. European Journal of Medical Research. 2013; 18(1): 40. doi:10.1186/2047-783X-18-40.
11. Oberweis BS, Cuff G, Rosenberg A, Pardo L, *et al*. Platelet aggregation and coagulation factors in orthopaedic surgery. *Journal of Thrombosis and Thrombolysis*. 2014; 38 (4): 430-438.
12. Zacharia G, Walczyszyn BA, Lee D, Stoffels G, *et al*. Characteristics of the post-surgical decreases in platelets counts in orthopaedic patients. *Blood*. 2016; 128: 2554.
13. Moyes AJ, Lamb RM, Ella-Tongwiis P, Pushkaran A, *et al*. A pilot study evaluating changes to haematological and biochemical tests after Flexible Ureterorenoscopy for the treatment of kidney stones. *PLOS ONE*. 2017; 12 (7): e0179599. https://doi.org/10.1371/journal.pone.0179599.
14. Hughes SF, Thomas-Wright SJ, Banwell J, Mushtaq S, *et al*. Are urological patients at increased risks of developing haemostatic complications following shock wave lithotripsy (SWL) for solitary unilateral kidney stones? European Urology Supplements. 2014; 13 (1), e816. doi:10.1016/S1569-9056(14)60804-6.
15. Hughes SF, Hendricks BD, Edwards DR, Maclean KM, *et al*. Total hip and knee replacement surgery results in changes in leukocyte and endothelial markers. Journal of Inflammation. 2010; 7 (2). doi:10.1186/1476-9255-7-2.
16. Hughes SF, Jones N, Thomas-Wright SJ, *et al*. Shock wave lithotripsy, for the treatment of kidney stones, results in changes to routine blood tests and novel biomarkers: a prospective clinical pilot-study. *Eur J Med Res*. 2020; 25: 18. https://doi.org/10.1186/s40001-020-00417-2.
17. Hughes SF, Moyes AJ, Lamb RM, *et al*. The role of specific biomarkers, as predictors of post-operative complications following flexible ureterorenoscopy (FURS), for the treatment of kidney stones: a single-centre observational clinical pilot-study in 37 patients. *BMC Urol*. 2020; 20. https://doi.org/10.1186/s12894-020-00693-4.