



The Effect of Uncomplicated Knee Arthroscopy on C-reactive Protein and Erythrocyte Sedimentation Rate

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Abstract

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BACKGROUND: Anticipated changes in erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) following uncomplicated knee arthroscopy have not previously been described.

AIM: We aim to identify these values to aid the management of patients who re-present with a suspicion of infection.

MATERIALS AND METHODS: Patients between 18 and 50 years undergoing day-case arthroscopic knee surgery under the care of the senior authors were recruited. Patients undergoing any bony intervention and those with a known inflammatory arthropathy were excluded from the study. Ethical approval was granted and patients consented to the study. ESR and CRP measurements were performed immediately prior to surgery, then at 1, 7, and 14 days postoperatively.

RESULTS: A total of 29 patients consented to the study. A full set of results were achieved for 17 patients. There was a significant increase in CRP on day 1 and day 7 following knee arthroscopy with a mean increase of 4.55 mg/L ($P = 0.003$) on day 1 and 1.78 mg/L ($P = 0.026$) on day 7. ESR did not change significantly at any of the measured points. The maximum value for CRP was 16 mg/L on day 1 and 11.5 mg/L on day 7. All CRP measurements had returned to baseline (<5 mg/L) by 14 days.

DISCUSSION AND CONCLUSION: Our study suggests that CRP measurement is a useful tool in the investigation of possible joint infection following simple knee arthroscopy. Continued elevation of CRP beyond 14 days or any significant elevation is not usual and suggests an abnormal post-operative recovery, which should prompt further investigation.

Introduction

Knee arthroscopy is one of the most commonly performed orthopedic procedures in the United Kingdom, with an annual rate of 9.9 / 10,000 population [1]. Knee arthroscopy is generally considered minor surgery, most patients are discharged on the same day as surgery and the reported complication rates are low [2], [3]. Despite the overall low risk of complications knee arthroscopy can be complicated by post-operative infection. This can be a devastating condition and if unrecognized may be associated with significant morbidity or mortality. The risks of septic arthritis complicating knee arthroscopy are very low and have been variously reported at 0.15–0.84% [3], [4]. In their review of 301,701 knee arthroscopies Jameson *et al.* (2011) reported a 30-day re-admission rate of just 0.64% for any complication [1].

For patients presenting with a clinical suspicion of post-operative infection, hematological investigations commonly form part of their initial assessment. This may include measurement of inflammatory markers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). These markers are not specific to infection and surgery in its self may cause them to rise which

can make post-operative interpretation of CRP and ESR changes challenging. The previous studies have analyzed these markers in patients presenting with clinical suspicion of a primary septic arthritis as well as following hip and knee arthroplasty. For these patients ESR levels >30 mm/h have been described as abnormally elevated [5] and Ernst *et al.* (2010) in a review of 44 proven septic joints demonstrated a mean ESR of 57 and a mean CRP of 13 [6]. Overall, the evidence suggests ESR to be a poor marker of joint infection [5], [6], [7] with reported sensitivities ranging from 75% to 96% [5], [7] and specificity as low as 11% [7]. By contrast CRP is considered a better diagnostic aid in the detection of joint infection particularly in the early post-operative period [6], [8], [9] due its rapid post-operative rise and relatively rapid fall. After uncomplicated knee arthroplasty CRP levels have been shown to peak on day 2 [8], [9] and return to normal by 21 days [8]. Conversely ESR is typically slow to rise, reaches peak levels by day 5 and frequently remains elevated several months to a year later [8], [9].

Similar changes in CRP and ESR have been demonstrated following anterior cruciate ligament (ACL) reconstruction with CRP peaking on day 3 [10], [11] and returning to normal faster than ESR. Wang *et al.* (2014) reported the optimal thresholds

for predicting infection following ACL reconstruction to be a CRP value of 41 mg/L and an ESR value of 32 mm/h [12].

While there is published data related to ESR and CRP changes after knee arthroplasty or ACL surgery, we were unaware of any such data indicating how these may alter after simple arthroscopic surgery. An extensive literature search of the MEDLINE and EMBASE databases including the terms; CRP, ESR, meniscectomy, uncomplicated, and knee arthroscopy revealed no published data on the expected values of these investigations following uncomplicated arthroscopic knee surgery.

For knee arthroplasty and ACL surgery, the measurement of inflammatory markers has been shown to be of value in the diagnosis of post-operative infection but with current evidence and a lack of "baseline" data it is unclear what values of CRP or ESR may be suggestive of this complication after simple knee arthroscopy.

The purpose of our study is to define the expected changes for both ESR and CRP following uncomplicated knee arthroscopy, thereby providing a "baseline" and allowing determination of values which may be considered abnormal. We hypothesized that in uncomplicated knee arthroscopy there would be no significant rise in either CRP or ESR.

Materials and Methods

Patients between 18 and 50 years of age undergoing single sided, simple day-case arthroscopic knee surgery under the care of the senior authors were prospectively recruited to the study. The term "simple" is used to identify patients not requiring any bony procedure such as micro-fracture or bone tunnel preparation. This excludes all patients undergoing ligament reconstruction, meniscal transplant surgery, and arthroscopic fracture or osteochondral fixation. This surgery includes arthroscopic meniscectomy, meniscal repair, or removal of loose bodies. Patients <50 years of age were selected in an attempt to reduce the number of medical comorbidities which may cause a pre-operative elevation in CRP or ESR.

Exclusion criteria included

Patients undergoing bilateral surgery or any bony procedure, patients with a diagnosis of an inflammatory arthropathy or any other inflammatory condition, patients taking any immunosuppressive medication, patients unable to understand English or give written consent and those with elevated inflammatory markers preoperatively.

The study was reviewed and approved by our regional Research Ethics Committee.

Eligible patients were approached preoperatively at their outpatient assessment and invited to participate. They were given verbal and written details of the study and patients who agreed to participate gave written consent.

Venipuncture for ESR and CRP measurement was performed immediately before surgery, and then repeated at day 1, 7, and 14 postoperatively.

A pilot study was conducted between November 2011 and July 2012. Further patients were then recruited between May 2015 and October 2016.

All data were collected utilizing a Microsoft Excel (Microsoft Corporation) worksheet and statistical analysis was conducted using IBM® SPSS® Statistics software (Version 24). Before starting the study, statistical advice was sought from the University of Sheffield statistics department who suggested a one sample *t*-test to determine a significant difference between pre-operative and post-operative levels. Confidence intervals of 95% were used.

Results

In total, 29 patients consented to be included in the study. Incomplete sets of data were achieved for eight patients as they failed to return for all blood tests and were therefore excluded from the study. One patient had a suspected aspiration on induction of anesthetic, one underwent ACL reconstruction, one had elevated CRP and ESR of unknown cause before surgery, and one patient had an inflammatory condition. All of these patients were also excluded leaving complete data for 17 eligible patients.

None of the 17 patients had a recognized complication following their surgery and all reported an uneventful and satisfactory recovery.

A normal value for CRP in our institution is 0–5 mg/L. No patient included had a CRP preoperatively of ≥ 5 . In 7 patients, there was an elevation >5 mg/L on day 1 postoperatively. The highest of these was 16 mg/L. At 1 week, two results were abnormal, with a maximum value of 11.5 mg/L. In all patients, the value returned to <5 mg/L at 2 weeks (Chart 1).

The mean value for CRP preoperatively was 1.21 mg/L. Using a one-sample *t*-test analysis, there was a significant increase on day 1 of 4.55 (95% CI 1.73–7.37 $P = 0.003$), however, in clinical practice this is a small rise. The difference at day 7 was even less at 1.78 (95% CI 0.24–3.32 $P = 0.026$) and by day 14 there was no significant difference (95% CI -0.24 –1.26 $P = 0.058$).

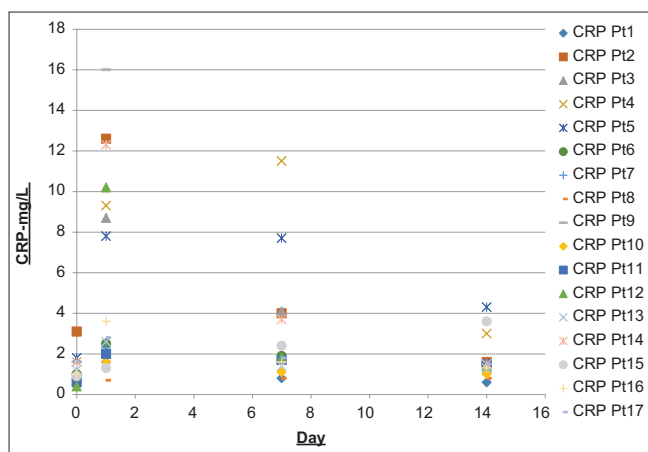


Chart 1: Change in C-reactive protein results per patient

For ESR, the normal range is 1–10 mm/h. No patient had an abnormal pre-operative test and only two patients had an increase on day 1 > 10 mm/h. In contrast to CRP, both of these levels remained >10 mm/h at 1 week. At 2 weeks one remained >10 mm/h and the other was below the pre-operative level. A one-sample *t*-test analysis demonstrated no significant difference at any point (1 day $P = 0.369$, 7 days $P = 0.057$, and 14 days $P = 0.357$). For most patients, ESR does not rise significantly within the first 2 weeks after simple knee arthroscopy (Chart 2).

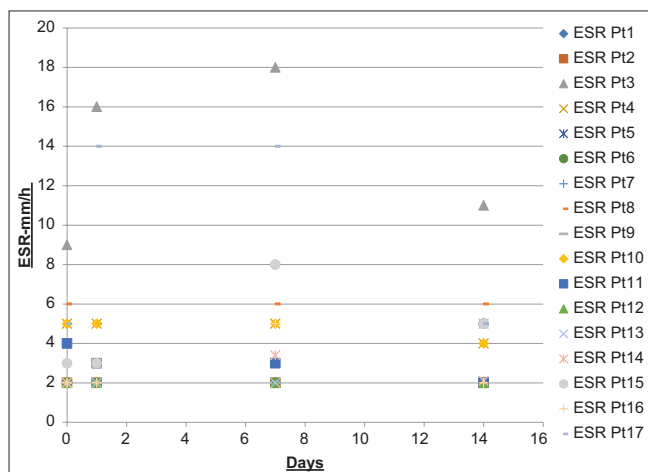


Chart 2: Change in erythrocyte sedimentation rate results per patient

Our study shows that following uncomplicated day case knee arthroscopy there may be a small rise in CRP but by 14 days after surgery any increase returns to normal levels. ESR is less likely to rise, but, if it does it may remain elevated after 14 days. We rejected our null hypothesis that neither CRP nor ESR alters after knee arthroscopy.

Discussion

ESR and CRP are frequently used as part of the assessment of patients with a potential

joint infection after surgery. ESR and CRP are inflammatory markers that may be elevated for a number of reasons including surgery itself but not specific to infection.

After major joint surgery such as total knee arthroplasty (TKA) large rises in ESR and CRP may be anticipated even in patients in whom recovery is uncomplicated. Less is understood about expected changes in ESR and CRP after minor knee surgery. There is a paucity of literature indicating what may be considered a normal “post-operative” rise in either CRP or ESR after knee arthroscopy making interpretation of these markers difficult in the assessment of a patient with a potential complication of their surgery.

Changes in CRP and ESR following arthroscopic ACL reconstruction have been studied previously [10], [11], [12]. Margheritini *et al.* [10] found that both CRP and ESR were markedly elevated after ACL reconstruction, peaking between days 3 and 7, with CRP returning to normal more rapidly than ESR. Calvisi *et al.* [11] corroborated these results for CRP, demonstrating a significant increase on day 1, with a peak on day 3, improving on day 7, and a return to normal by 15 days.

Wang *et al.* [12] published results of 122 patients undergoing ACL reconstruction, of whom 39 developed post-operative septic arthritis and reported a significantly higher CRP and ESR in patients with a septic joint compared with a uncomplicated recovery. They suggested threshold values of 41 mg/L for CRP and 32 mm/h for ESR were optimally sensitive and specific for distinguishing a septic from a normal joint after arthroscopic ACL reconstruction.

The current evidence would, therefore, suggest that CRP and ESR are both elevated after uncomplicated arthroscopic ACL reconstruction, but in an infected joint these values may be significantly higher.

While there is evidence guiding what elevation of CRP or ESR after TKA or ACL surgery may be considered normal and what may suggest post-operative infection before our study, there were no data on these changes after simple knee arthroscopy. Typically simple knee arthroscopy may be considered a minor procedure that is of relatively short duration and patients recover quickly. It may, therefore, seem logical to assume that CRP and ESR changes would be less after these procedures compared with ACL surgery or TKA.

We set out to define a range of CRP and ESR values that may be considered a normal response to surgery in an attempt to guide clinicians using these markers in the assessment of patients with a possible post-operative infection after knee arthroscopy. Our results suggest that following knee arthroscopy a markedly elevated CRP (above 16 mg/L) or a CRP that remains elevated after 14 days should not be attributed

to a normal response to surgery and warrants further investigation.

ESR is less easy to predict and after uncomplicated knee arthroscopy typically does not rise but rarely it may and remain elevated after 14 days. This makes interpretation of ESR changes after knee arthroscopy less useful in the assessment of a post-operative infection.

The authors acknowledge that the relatively small cohort of patients in this study is a limitation. Recruitment of eligible patients was difficult, we believe due to the requirement for additional venepuncture and hospital attendances after the procedure. We also recognize that these results may not be applicable to patients with an elevated CRP before surgery. Care should be exercised in interpreting inflammatory makers in patients with a diagnosed inflammatory condition; however, this probably applies after all surgical procedures.

Conclusion

CRP measurement may be a tool used in the investigation of a patient for possible joint infection after simple knee arthroscopy. After knee arthroscopy elevation of CRP beyond 14 days or a significant elevation is not usual and merits further assessment.

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