TITLE: Retrospective evaluation of factors influencing transfusion requirements and outcome in cats with pelvic injury (2009–2014): 122 cases

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Abstract:

Objective – To characterize a population of cats with pelvic trauma and evaluate factors influencing transfusion requirement and outcome.

Design – Retrospective case series (2009-2014)

Setting – University teaching hospital

Animals - One hundred and twelve client-owned cats with pelvic trauma

Interventions – None

Measurements and main results - Twenty-one (18.8%) cats received a transfusion. Most cats required only one fresh whole blood transfusion (85.8%). Packed cell volume at admission was significantly lower in cats that required transfusion but was not associated with hospitalization time or survival to discharge. Increasing Animal Trauma Triage (ATT) score at admission was significantly associated with transfusion requirement (p=0.0001) and non-survival to discharge (P=0.03). Number of pelvic fractures was not associated with transfusion requirement but cats with sacroiliac luxations and pubic fractures were more likely to require a transfusion (p=0.0015 and p=0.0026 respectively). However, fracture type was not associated with survival to discharge. Most cats (86%) required a surgical procedure and half of transfusions were administered pre-operatively. No surgical comorbidities were associated with transfusion requirement or survival. Transfusion requirement was associated with longer length of hospitalization but not survival to discharge.

Conclusions – Transfusion requirement in this population of cats with pelvic fractures was fairly high. Transfusion requirement was associated with lower packed cell volume, higher ATT score at admission, longer length of hospitalization and certain types of pelvic fractures. Transfusion requirement was not associated with surgical co-morbidities, surgical intervention or survival to discharge. Lower ATT score at admission was associated with survival to discharge.

Abbreviations:

ATT Animal Trauma Triage Score

ISS Injury Severity Score

FWB Fresh Whole Blood

PCV Packed Cell Volume

AFAST Abdominal Focused Assessment with Sonography for Trauma

***Introduction**:*

Pelvic fractures in cats account for approximately 25% of all reported fractures and are usually a result of high impact blunt trauma.[1] These forces, when applied to the rigid box-like structure of the pelvis, often result in multiple bilateral fractures and pelvic instability. Consequently, pelvic hemorrhage can occur, originating from bone or from disruption of local vasculature. [2]

High impact trauma is also commonly associated with injury to other body systems. These sites may act as additional sources of hemorrhage. Injury to the thorax and abdomen in particular are thought to contribute significantly to morbidity and mortality. Additional soft tissue, urinary tract, and neurologic injuries are also encountered. [3]

Traumatic pelvic fractures in people are associated with high mortality rates in the first 24 hours. This is most commonly associated with acute, severe hemorrhage from the pelvis or abdomen.[4-6] Predicting transfusion requirement and outcome in this patient group has therefore received much attention. Age [7], presence of shock on arrival [7-10] and admission hematocrit, [8,10] have all been associated with requirement for blood products. However, multiple large studies have been unable to consistently predict transfusion requirement based on the type of pelvic fracture, with various classification schemes being trialed based on direction of force, degree of displacement and rotational stability. [6-8,11,12] This is likely because isolated major hemorrhage from the pelvis is thought to be rare. [4,13] Overall assessment of concurrent injuries has instead been shown to be more useful in predicting transfusion requirement and mortality in human pelvic fracture patients. [5,6,13,14] This is often presented as an Injury Severity Score (ISS): an anatomical scoring system of 6 body regions to numerically describe the overall severity of injury.[15] Mortality in this patient group has been associated with age [6,14,16], admission hematocrit/hemoglobin [5], systolic arterial blood pressure [5,14,17] and transfusion requirement. [6,16,18] Pre and post operative hemoglobin levels have been associated with length of hospitalization.[19]

Although there is little information regarding the use of transfusions in feline trauma patients, it is the

perception of the authors that acute, severe hemorrhage is an uncommon presentation in cats with pelvic fractures. However, whilst rarely needed during initial resuscitation, blood transfusions are considered to be a fairly frequent requirement to stabilize patients for further interventions.[2]

Up to 58.6% of cats with pelvic fractures have been reported to have concurrent injuries, [20] and the presence of abdominal injury or soft tissue trauma has been associated with non-survival to discharge in general feline trauma cases. [3] However, to the authors' knowledge, the incidence of significant hemorrhage, and consequent requirement for transfusion and outcome prediction, has not been specifically investigated in feline patients. The aim of the current study was to perform a retrospective review of cats that sustained traumatic pelvic fractures, to document their need for blood transfusion and to identify predictors of transfusion requirement and outcome. Our principal null hypothesis was that receiving a blood transfusion would have no impact on survival to discharge in cats with pelvic trauma.

Materials and Methods:

The medical records database at a university teaching hospital was searched for cats presenting with pelvic trauma between January 2009 and January 2014. Cats were eligible for study inclusion if they had sustained any bony pelvic injury (fractures and/or sacroiliac luxation), had complete medical records (detailing initial physical examination findings, packed cell volume, treatment given and patient outcome), and had radiographs or computed tomography images of the pelvis reviewed at the time by a board certified diagnostic imager. Age, sex, breed and body weight were recorded. Both primary and referral cases were included. An Animal Trauma Triage Score (ATT) [11], an anatomical numerical scoring system for assessing polytrauma, similar to the ISS in people, was determined retrospectively based on the physical examination findings at the time of presentation.

A blood transfusion was defined as administration of any hemoglobin-containing blood product including Oxyglobin™[a]. The type, and number, of transfusions provided, whether they were administered pre, intra or post-operatively and the packed cell volume (PCV) prior to transfusion were recorded for all cases.

The types of pelvic injury documented on the imaging reports were recorded as sacroiliac luxation, sacral fracture, ilial fracture, acetabular fracture, ischial fracture, and pubic fracture. Management of pelvic fractures (surgical or conservative treatment) was also recorded. Additional co-morbidities requiring surgical intervention were determined from the medical records, then classified by body system affected (cardiovascular, neurological, urinary, integumentary, gastrointestinal, ocular). Integumentary systems injuries were included if abrasions, partial thickness lacerations, or full thickness lacerations involving deep tissues but without penetration into a body cavity were noted in the medical record.

Length of hospitalization and survival to discharge were recorded. If a patient died, then it was noted whether this was secondary to cardiopulmonary arrest or euthanasia.

Statistical Methods:

For statistical analysis of study objectives, cats were classified as either transfusion status positive or negative, whether they received any surgical intervention and whether they survived to discharge. Population characteristics (age, ATT score, presence of surgical co-morbidities, type of pelvic fracture and PCV at admission) and outcome criteria (requirement for surgery, length of hospitalization and mortality) were then compared between transfusion status, requirement for surgical procedure and survival to discharge groups.

Continuous data sets were analyzed for normality using the Shapiro Wilk test. A Student's t-test was used to compare the means of continuous data. Categorical data were presented as median and range. A Fisher's exact test was used to compare categorical data. Ordinal data was presented as median and range. Chi-square for trend analysis was used to examine the relationship between ATT and requirement for blood transfusion or survival. The remaining data were presented descriptively. Statistical analysis was performed using Graphpad software[b]. Results were considered significant with a P value <0.05.

Results*:*

One hundred and twelve cats were identified with pelvic fractures over the study period. All data could be obtained from the medical records and therefore no cats were excluded from the study. The cats had a median age of 40 months (range 4 months to 192 months). There was no significant difference between the ages of the cats based on requirement for transfusion, surgical intervention or survival to discharge. There were more males than females (63 and 49 respectively) and 92.8% were neutered. Median weight was 4.18kg (range 2.2 – 6.18kg). Fourteen breeds were represented with Domestic Shorthairs being the most common (63.4%). The majority of cases were un-witnessed trauma but thought to be vehicular related. Seventy-nine cats (70.5%) were presented to a primary care practice before referral.

Twenty-one (18.6%) cats received a blood transfusion. Average time from admit to transfusion was 3.6 days (range 1 to 6 days). All cats that received a transfusion underwent surgery, with 12 transfusions (50%) being administered pre-operatively, 3 intra-operatively (12.5%) and 9 post-operatively (37.5%). Eighteen cats received one transfusion (85.8%) and 3 cats received 2 transfusions (14.2%). Eighteen cats received fresh whole blood (FWB) alone and 3 cats received both FWB and Oxyglobin™. Cats receiving Oxyglobin™ all went on to receive a FWB transfusion.

The median ATT score for all cats was 4. Median ATT score for cats receiving a transfusion was 6 (range 3-11) compared to 4 (range 0-9) for those not receiving a transfusion. A chi-square test for trend showed a significant linear association between increasing ATT at admission and proportion of cats receiving a blood transfusion (P = 0.0001). Median ATT score for cats surviving to discharge was 4 (range 0-10) compared to 6 (range 2-11) in those that did not survive. A chi-square test for trend showed a significant linear association between a lower ATT score at admission and survival ($P < 0.03$).

In total, 96 of 112 cats (86%) had a surgical procedure. The majority of cats (75%) underwent fracture stabilization. Some of these required an additional procedure with twenty-five cats (22.3%) undergoing surgery for injuries sustained to another body system. Fifteen cats (13.4%) sustained skin wounds and 9 cats (8.0%) had urinary tract trauma requiring surgical management. One cat required an enucleation (0.9%). There was no significant difference between the frequency of surgical co-morbidities in the transfusion or survival groups. There was also no significant difference between the transfusion requirement or the ATT scores for cats that did or did not undergo a surgical procedure.

Diagnostic imaging revealed 76 out of 112 cats had sacroiliac luxation(s) (67.9%), 58 had pubic fractures (51.8%), 54 had ischial fractures (48.2%), 45 had ilial fractures (40.2%), 19 had acetabular fractures (17.0%), 11 had coxofemoral luxations (9.8%), 6 had lumbosacral luxations (5.3%) and 6 had sacral wing fractures (5.3%). There was no significant difference in the number of pelvic fractures in those cats that required a transfusion and those that didn't. However, significantly more cats that required a transfusion had sacroiliac luxation and pubic fractures compared to those cats that weren't transfused (p=0.0015 and p=0.0026 respectively). Type of pelvic fracture was not associated with survival to discharge.

The mean PCV at admission was significantly lower in the cats that required transfusion (23% [SD 6.6%]) compared to the group that weren't transfused (29.2% [SD 7.0%]) (p=0.0005). There was no correlation between PCV at admission and hospitalization time, irrespective of transfusion status. PCV was not associated with survival to discharge. When comparing the PCV of first opinion and referral cases, for the cats that were transfused, the mean PCV was not significantly different (first opinion = 25.6% [SD=8.5%]; referred = 20% [SD=6.3%]). For the cats that weren't transfused, the PCV was significantly different (first opinion = 35.5% [SD=6.2%]; referred = 27.4 [5.8%]; p<0.0001).

All cats were hospitalized for at least 24 hours and 102 cats survived to discharge (91.1%). Mean length of hospitalization for all cats was 7.0 days (SD=4.0). After excluding those that were euthanized, length of hospitalization was significantly longer in cats that received a transfusion (mean=9.4days [SD=5.2days]) compared to those that didn't (mean=6.4days [SD3.5days]) (p0.002). Of the 10 cats that did not survive, 2 animals underwent cardiorespiratory arrest and the remainder were euthanized. Only 4 out of the 10 underwent a surgical procedure (two underwent fracture stabilization; two other cats had cystotomy tubes placed). Requirement for transfusion or surgery was not associated with survival to discharge.

Discussion:

The results of this study indicate that, in this referral population of cats with pelvic fractures, transfusion requirement was fairly high, with 18.6% of cats requiring a FWB transfusion during hospitalization. Transfusion requirement was associated with lower PCV and increased ATT score at admission, as well as sacroiliac luxation and pubic fractures. Transfusion requirement was not associated with surgical co-morbidities, surgical intervention or

158 survival to discharge but was associated with longer length of hospitalization. Overall survival to discharge was high
159 and a higher ATT score at admission was the only finding associated with non-survival to discharge.

160 The signalment in this population was similar to that reported in other studies, with younger, male cats
161 being most commonly represented. [21,22] Age was not associated with transfusion requirement or survival to
162 discharge as has been reported in human studies. This is likely because the geriatric population in this study was
163 small, with only 5.4% of cats greater than 10 years old. With a small geriatric component, pre-existing age-related
164 co-morbidities that could impact the ability to tolerate anemia, or impact survival, were difficult to evaluate.

165 Nearly 1 in 5 cats required a transfusion, although no transfusions were administered in the first 24 hours
166 and no cat received more than one FWB transfusion. Transfusion is therefore unlikely to be required for immediate
167 resuscitation in this population as all cats survived at least 24 hours from presentation. This is useful information for
168 the clinician discussing financial implications with owners and also when planning blood product supplies. It may
169 also explain why transfusion requirement had no association with mortality in contrast to human medicine. People
170 with pelvic fractures can require multiple transfusions during initial stabilization and this may ultimately result in a
171 much greater proportion of the circulating blood volume being replaced. This can predispose to a coagulopathic
172 state and increased mortality.[23] Cats that received a transfusion were hospitalized for significantly longer than those
173 that did not. This may be associated with the time required time required to procure FWB or overall injury severity,
174 as cats requiring a transfusion also had a higher ATT score.

175 The finding that the ATT score was associated with transfusion requirement and also survival to discharge
176 is similar to the relationship between ISS and transfusion requirement and mortality in people with pelvic fractures.
177 A previous study also demonstrated this relationship in dogs.[26] This same canine study also suggested that
178 hemoperitoneum, as detected by abdominal focused assessment with sonography for trauma (AFAST) scans, is a
179 common finding in canine pelvic fracture patients with high ATT scores. [26] Therefore, although the cats in this study
180 were not routinely screened for hemoabdomen, given the data available in dogs, inclusion of serial AFAST evaluation
181 may have further helped identify cats at risk of requiring a transfusion.

182 In this population, only 50% of all transfusions were administered preoperatively. It is unclear given the
183 retrospective nature of this study whether this was a result of difficulty obtaining feline blood products, or whether
184 the patients truly did not require blood until intra- or post-operatively. One concern, if related to difficulty obtaining

the blood for transfusion, is that this could mean administration was not always at the optimum time for the patient. Unlike in people and dogs, there are no widely available storage facilities for feline blood products in the United Kingdom and much of Europe. Transfusion availability therefore often relies on the location of a suitable donor and collection of blood on demand, both of which can significantly delay transfusion administration. Given these impediments to transfusion, being able to better predict transfusion requirements in feline trauma patients would aid in their timely management, especially if transfusions are required prior to further interventions.

The finding that cats requiring transfusion had significantly lower PCVs on presentation may help to prompt clinicians to consider that significant hemorrhage has occurred and blood transfusion may be required. However, PCV alone is not the sole indication for transfusion administration, and it should also be remembered that this value will be influenced by volume and hydration status. Studies in dogs and humans have shown a better correlation between lactate or base excess and transfusion requirement and mortality compared to initial PCV. [24] [25]

The major cause of anemia in this population of cats was thought to be blood loss due to the initial trauma that caused the pelvic fracture. However, critically ill cats presenting secondary to trauma may develop anemia via a variety of pathways including frequent phlebotomy, oxidative damage and a poor regenerative response. In a retrospective study, 33% of critically ill cats developed anemia whilst hospitalized. Given over one third of transfusions were given post-operatively, it's likely anemia was multifactorial in these patients. Intra-operative factors such as surgical time, blood loss or anesthetic factors, which could not be determined retrospectively, may also have had an impact.

Concurrent surgical injuries were seen in 22.3% of this population. Although the frequency of surgical co-morbidities was not associated with transfusion status or survival to discharge, they may have implications for early stabilization of patients. For example, in this study, all trauma to the urinary tract was managed surgically rather than medically and therefore cats required stabilization prior to/in order to undergo general anesthesia. Only surgical co-morbidities were included in this study as they were more consistently recorded and described in the patient records. However, in omitting medical comorbidities from the study, which are more variable in severity and therefore difficult to consistently recognize in a retrospective study, we could have failed to identify other factors that may have influenced outcome.

The finding that sacroiliac luxations and pubic fractures were both seen more frequently in the transfusion group could theoretically be useful. However, as previously discussed, significant hemorrhage from the pelvis alone is thought to be rare in people and concurrent injuries are more useful in predicting transfusion requirement. Further studies are required to determine if this is also the case in cats, although the finding that higher ATTs were associated with transfusion requirement suggests this may be possible. Given the overall frequency of sacroiliac luxations and pubic fractures in this population, it is also not feasible to use these injuries alone to predict transfusion requirement clinically. However, they should perhaps prompt more thorough investigation of pelvic and extra-pelvic hemorrhage and closer monitoring of PCV.

Survival to discharge in this population was high at 91% and our null hypothesis was rejected as no association was found between survival and transfusion requirement. The low mortality rates seen in this study are consistent with other veterinary studies, including a report of 12-14% mortality in dogs presenting with blunt trauma. [27] However, cats with the most severe trauma may die very soon after the injury, therefore never presenting to a veterinary facility for treatment. As such, this study may be a poor representation of the overall population of cats that suffer pelvic trauma and survival rates may not be as high. Furthermore, the ATT scores of referral cases may also not reflect the initial primary care assessment and may have been significantly higher in some cats, depending on the varying levels of care prior to arrival at our facility.

This study has a few other limitations to note. It was not possible to access digital radiographs between 2009 and 2011. Therefore, although each radiograph was reported by a board certified diagnostic imager, none of the radiographs were reviewed specifically for this study. It was therefore not possible to investigate whether specific characteristics of sacroiliac luxation and pubic fractures, for example, degree of cranio-caudal or medio-lateral displacement provide better prediction of transfusion requirement, hospitalization time or survival. However, in dogs, increased lateral pelvic compression was not associated with increased intra-abdominal injury (including hemoperitoneum) and in humans the literature is inconsistent. Although not necessarily required for surgical planning, CT would also have offered better analysis of pelvic fractures compared to radiography.[25]

A further limitation of this study is that more cats may have benefitted from, rather than required, blood products but may have not received them due to limited resources. This could be from a lack of synthetic product availability, variable presence of donor colonies and reliance on client owned donors. Given there are no

238 standardized transfusion 'trigger' protocols in veterinary medicine, clinician decision making about when to
239 transfuse patients also introduces some variability.
240
241 Conclusions:
242 This study highlights that cats presenting with pelvic fractures require transfusion fairly frequently, although in
243 this population, no cat required more than one FWB transfusion. Transfusion requirement was associated with lower
244 PCV and higher ATT score on admission; presence of sacroiliac luxations and pubic fractures and longer
245 hospitalisation times. Transfusion requirement was not associated with surgical co-morbidities or surgical
246 intervention. This data supports our null hypothesis as only ATT score was associated with survival to discharge and
247 not transfusion requirement.
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252 **Footnotes**:
253 a. Oxyglobin ™ Biopure Corporation, Cambridge, MA
254 b. GraphPad Prism 7, GraphPad Software, La Jolla California USA
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