The hidden cost of gun violence: a case report and scoping review of the relationship between gun violence and infertility

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Title: The hidden cost of gun violence: a case report and scoping review of the relationship between gun violence and infertility

Running Title: Gun violence and infertility

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Abstract

Objective: To study (1) the existing data on the relationship between penetrating abdominopelvic injuries and fertility (2) guidance on managing fertility concerns of these patients using a case report and scoping review.

Design Case report and scoping review

Setting Not applicable

Patients People who have experienced abdominopelvic trauma from gun violence or in the course of combat.

Interventions None

Main Outcome Measures We extracted case report data from electronic health records. We performed a scoping review using Pubmed and SCOPUS. Search terms were related to penetrating abdominopelvic trauma, gunshot wounds (GSW), war and fertility/infertility. We evaluated the study year, age and race, mechanism of injury, fertility outcomes and how fertility concerns were addressed with patients who experienced penetrating abdominopelvic trauma

Results:
Case report: The couple had ten years of infertility. The male partner experienced an abdominopelvic GSW prior to attempting to conceive. After evaluation, he was diagnosed with retrograde ejaculation. He recalled being advised that his GSW might affect his future fertility. The couple has discontinued care.

Scoping Review: 879 sources were identified; 25 studies were included in the review. Among studies in the United States, the majority of patients included were African American.

Eighty-eight percent (n=22) of sources acknowledged the importance of fertility or used fertility-related outcome measures. One study commented on how to address fertility concerns with victims of abdominopelvic penetrating trauma.

Conclusion: There is a paucity of data on the intersection of penetrating abdominopelvic injuries and fertility or guidance on how to discuss fertility issues with patients.

Keywords: infertility, gun violence, gunshot wounds, trauma
Introduction

Gun violence is a pervasive issue in the U.S. There are over 80,000 visits to the emergency room each year for non-fatal firearm injuries and these injuries are most commonly the result of an assault (1). Approximately 20% of firearm assaults result in abdominopelvic injuries (2). Penetrating abdominopelvic injuries such as gunshot wounds may impact future fertility, especially when urologic or gynecologic in nature. However, current data is limited on how to manage patients with penetrating abdominopelvic injuries to optimize future fertility. Neither the American Urologic Association urotrauma guidelines, the American Association for the Surgery of Trauma or the American Society for Reproductive Medicine currently provide guidance on how to counsel patients about the potential fertility issues associated with these injuries (3). The American College of Obstetricians and Gynecologists provides a guideline, “Caring for Patients Who have Experienced Trauma” however trauma is broadly defined to include both physical and psychological harms in the document and there is no guidance on fertility related discussions (4).

Understanding the long-term effects of gun violence on fertility may identify an unrecognized contributor to infertility. Using age and sex adjusted life expectancy rates, cause of death, and birth rates, investigators Wilson and Daly demonstrated a regional relationship between lowered life expectancy and earlier reproductive timing in zip codes most affected by gun violence in Chicago in the 1980s and 1990s(5). Not only may gun violence influence behaviors, quality of life, and life expectancy, but it is also possible that it could directly influence the ability to conceive through the anatomic injuries obtained. In the United States, due to well-documented structural racism, people of color are disproportionately affected by gun violence (6) (7) (1)(2). Increasing provider awareness at all touch-points for gun violence victims from their primary care physicians to reproductive health sub-specialists could aid in the promotion of fertility health equity.

We present a case report that demonstrates the potential influence of penetrating trauma on fertility. Following this case report, we will present a scoping review with two objectives: first, to assess what data exists on the relationship between penetrating abdominopelvic injuries and fertility; second, to assess the available guidance on counseling and managing the fertility concerns of these patients.
Methods

Protocol

We followed the Preferred Reporting Items for Systematic Reviews and Meta-analysis Protocols (PRISMA) to conduct our scoping review. To be included in the review, we sought studies (case reports, case series, retrospective and prospective cohorts, case control studies, and reviews) that were closely aligned with our primary objectives. Included studies met the following criteria:

- Title or abstract included the mechanism of injury specified as gun violence or penetrating abdominopelvic trauma due to a violent act
- Title or abstract reports on outcomes related to the genitourinary tract or fertility
- Title or abstract discusses the management of these injuries
- Includes humans only
- English as primary language
- Full manuscript accessible at the time of the review
- No location restriction
- Publication range - Open

Studies meeting the following criteria were excluded:

- Full text unavailable
- Non-English
- Studies that do not comment on penetrating trauma and genitourinary injury or fertility outcomes
- Studies that specify spinal injury cord trauma as the primary trauma, despite consequent penetrating abdominopelvic trauma
- Studies focusing on intimate partner violence, sexual violence, marital violence, genital mutilation, domestic violence, domestic abuse, reproductive coercion, sexual abuse, interpersonal violence, rape or other forms of trauma
- Populations that included pregnant women
- Ethical or opinion pieces, legal proceedings

Sources were identified through Pubmed and SCOPUS searches conducted from June 1st, 2021 to July 15th 2021, using the search MeSH terms:
"Wounds, Penetrating" AND "Infertility"

"Wounds, Penetrating" AND "Fertility"

"Wounds, Gunshot" AND "Infertility"

"Wounds, Gunshot" AND "Fertility"

"War-Related Injuries" AND "Infertility"

"War-Related Injuries" AND "Fertility"

"Gun Violence" AND "Infertility"

"Gun Violence" AND "Fertility"

Potential sources were evaluated by two reviewers AA and AN. Any discrepancies about study inclusion were resolved by discussion between reviewers. Relevant data from included sources was recorded in a data charting form that included the authors, study title, country of origin, date retrieved, year the study was published, the population, primary results, and whether or not studies addressed fertility or made recommendations about fertility discussions. Studies were assessed for trends in addressing fertility issues and fertility counseling.

**Development of case report**

Relevant data about the patient were retrieved using an electronic medical record system. This included the primary concern, history and physical, and relevant labs and treatment. This case report (IRB21-1234) was exempt from the University of Chicago Institutional Review Board as a single case report excluding protected health information.

**Results**

**Case report**

**History of present illness**

The patient was a 37-year-old gravida 0 with ten years of primary infertility at the time of presentation. Five years prior to her presentation, she initiated a fertility evaluation that demonstrated unilateral tubal occlusion and bilateral hydrosalpinges (Table 1). Her male partner was not evaluated. At the time, she was informed that her likelihood of fertility was low. However, she decided that she and her partner would continue trying to conceive with regular
intercourse 3-4 times per week. The couple did not report any sexual dysfunction. After five additional years of trying to conceive, she presented to our clinic for additional fertility care.

The partner was a 42-year-old medically healthy male. He was the victim of gun violence and suffered an abdominal gunshot wound (GSW) that required an exploratory laparotomy although he does not recall what surgical procedures were performed. He had a daughter from a previous relationship conceived prior to his GSW injury. He was a smoker with no other toxic exposures. His semen analyses demonstrated teratospermia as well as low volume, asthenospermia and oligospermia with retrograde ejaculation (Table 2). After treatment with pseudoephedrine and sodium bicarbonate, his semen parameters improved marginally. The total motile count of 7.4 million in the final specimen was still suboptimal for intrauterine insemination.

Follow up

After reviewing results with the patient and partner, the partner recalled that at the time of his laparotomy for his gunshot wound, he was told that his injury was “very low” and that having children in the future may be difficult. This information was new to the female patient. The male partner was diagnosed with retrograde ejaculation. Two treatment approaches were offered. First, a trial of intrauterine insemination with treatment for retrograde ejaculation was proposed. Multiple ejaculates per insemination would be likely. The second treatment approach included in vitro fertilization (IVF) with preimplantation genetic testing for aneuploidy, interval bilateral salpingectomy after euploid embryos were obtained, and frozen embryo transfer of a single euploid embryo. The patient chose to do intrauterine insemination, initiated a cycle but neither she nor her partner presented for insemination. She has now decided not to pursue treatment.

Scoping Review

Selection of Sources of Evidence

879 sources were identified through searches of Pubmed and Scopus, or through examining the references of included studies. After 112 duplicates were excluded, 767 sources were examined for potential inclusion. 718 sources were excluded by their title or abstract and there were 6 studies excluded because the full text could not be retrieved. We reviewed the full text of forty-three studies. After review, eighteen studies were excluded for the following reasons: the mechanism of injury did not include gunshot or other penetrating abdominopelvic trauma (n=16) the study did not include humans (n=1), or the source was an editorial which was an excluded source (n=1). Twenty-five sources were included in the scoping review including case
reports/series (n=6), retrospective cohort studies (n=12), reviews (n=5), a case-control study (n=1) and a cross-sectional qualitative study (n=1) (Figure 1).

**Demographics**

Twenty-five studies and reviews met criteria to be included in the scoping review. These studies addressed the management of such injuries or fertility related outcomes. Among the included studies, the age range of patients affected by penetrating abdominopelvic trauma ranged from 5 to 83, although the majority of people were under 35 years of age. Nine of the sources included in the review came from the studies of veterans or victims of war (Table 3). Among studies in the United States, when race was reported, the majority of civilian patients affected by penetrating trauma were African American (8)(9). Mattocks et al performed a retrospective cohort study of women veterans deployed for Operations Enduring Freedom, Iraqi Freedom and New Dawn. Women in this cohort who were given an ICD-9 diagnosis of infertility also were significantly more likely to be young, obese, African American, or impacted by a service-related disability or sexual trauma (9).

**Female injuries**

Penetrating trauma to reproductive structures (uterus, fallopian tubes or ovaries) is rare and represented less than 0.1% of injuries in the National Trauma Databank (NTDB) between 2007 and 2015(10). In our review, we identified four studies that explicitly reviewed the female experience(11)(10)(12)(13). Rivas et al. conducted a retrospective cohort study of 313 women who had experienced gynecologic trauma reported to the NTDB between 2011 and 2013. The authors demonstrated that although most reported traumas were blunt trauma, 21% resulted from penetrating trauma. Most gynecologic trauma resulted in injury to the ovaries or fallopian tubes (74.8%) whereas the uterus was injured in a minority of cases (25.2%). Importantly, gunshot trauma more often resulted in salpingoophorectomy rather than attempting to repair the injured tissue. While this study shed light on the surgical approach to gynecologic traumas, it did not address how to discuss these injuries with patients or manage expectations around future fertility (11).

**Male Injuries**

In our review, the majority of studies examined the impact of violence and war on male fertility. Penetrating abdominopelvic trauma often involves the male external genitalia. Multiple sources described managing severe penetrating injuries to the scrotum with orchiectomy and in some cases bilateral orchiectomy (14)(15)(16). A general review of the epidemiology of genitourinary
trauma estimates that orchiectomy is required in 25-65% of patients with scrotal trauma (17). While uncommon overall, male genital injuries can result in significant long-term morbidity with fertility sequelae such as erectile dysfunction, hormonal dysfunction, primary spermatogenetic dysfunction, or psychological distress. Similar to the current literature on female injuries, our review did not identify studies that clearly discussed long-term management of these fertility issues in the post-trauma setting.

Management of injuries

The majority of included studies and reviews focused on the epidemiology of penetrating abdominopelvic injuries or surgical management of these injuries. Eighty-eight percent (n=22) of the studies acknowledged the importance of the injury to fertility or used fertility-related variables (potency, endocrine profile) as an outcome measure (Table 3). People with war-related injuries to pelvic structures often also experienced other injuries including limb amputations or traumatic brain injuries (18), (19). Civilian studies typically did not comment on additional injuries. Most urologic studies advocated for either scrotal ultrasounds and/or early exploration for clear testicular injuries.

Combat injuries

With advancements in surgical technique and improvements to body armor to protect the head and upper torso, the prevalence of people surviving complex pelvic injuries, commonly from improvised explosive devices, has increased (20). Consequently, a substantial proportion of studies included in this scoping review focused on veterans and victims of war (n=10). Exposure to war, either as a veteran or civilian victim of war, was associated with an increased risk of infertility in the studies included in this review when infertility was the primary outcome (n=3) (Table 3) (21)(9)(22). All combat-related studies commented on the potential relevance of abdominopelvic injuries on future fertility or used infertility and treatment success as a primary outcome (Table 3).

Interestingly, in a retrospective cohort study of veterans who served in Operation Iraqi Freedom and Operation Enduring Freedom, Janak et al noted that in their clinical practice, they "anecdotally identified previously fertile men who sustained severe blast injury to the pelvis and were (months or years later) subsequently found to have testicular atrophy and biopsy confirmed nonobstructive azoospermia despite no evidence of overt testicular injury at the time of initial presentation, presumably due to delayed effects from the initial blast injury. For many of these men paternity is no longer possible without the use of donor sperm, which is not a covered benefit
for current or former U.S. SMs." These observations raise the possibility that there may be long-term fertility consequences from abdominopelvic trauma related to blast injury even when injuries do not directly harm reproductive structures.

In contrast, a minority of sources in this review that included civilians did not address fertility concerns at all in their results or discussion (n=3)(Table 3).

Communicating fertility concerns

Although most studies acknowledged that fertility may be a concern after penetrating abdominopelvic trauma or combat related injuries, most studies (n=24) did not provide a framework for how providers might discuss the potential impacts of these injuries on future fertility or sexual function (Table 3).

One study from Lucas et al addressed how to disclose the nature of the penetrating reproductive injury with the patient. The authors of this qualitative study interviewed 13 men who experienced urogenital injuries while deployed by the United Kingdom. Common themes expressed by the men included a desire to understand the full impact of their injuries on their future fertility early in their treatment journey and valued learning about their injuries from professionals with expertise in this area. The majority of these men also rated the importance of their genital injuries higher than other combat related injuries such as limb loss. The authors advocated for fertility preservation once the injury is recognized, follow-up and comprehensive fertility and psychological care after these injuries (23).

No studies described a process of longitudinal follow-up to address fertility issues for patients with penetrating genitourinary trauma.

Fertility Interventions

Although the long-term fertility outcomes for people experiencing penetrating abdominopelvic trauma are extremely limited, some case reports and series focused on novel strategies to address infertility in this population. Techniques included zygote intrafallopian transfer or seminal vesical sperm aspiration for use with intracytoplasmic sperm injection with subsequent successful pregnancies (24)(25). The utility of certain fertility preservation techniques depends on the context of the injury. Trauma that occurs during combat may be anticipated and addressed with pre-deployment oocyte or sperm cryopreservation, whereas the options for civilian trauma are more limited. Fortunately, the field of infertility care has evolved to include many treatments
that would be successful in this population. However, the accessibility of these treatments is often limited since many who experience gun violence are also socioeconomically disadvantaged.

Discussion

This scoping review identified twenty-five studies and reviews that addressed penetrating abdominopelvic trauma, its management or implications for fertility related outcomes. Although injuries to reproductive organs after penetrating trauma are relatively rare in women, they represent about 3-10% of injuries among men (10)(12)(26). Among sources included in this review, there were associations between people experiencing war trauma and the incidence of infertility. However, no studies specifically explored a direct relationship between penetrating abdominopelvic trauma and infertility. The case reports included in this review often described direct trauma to the genitalia, sometimes with negative impacts to endocrine function or gametogenesis. It is possible that querying infertility in a larger cohort of people experiencing direct penetrating abdominopelvic trauma may reveal a clear relationship. Over the time period of the study, thousands of people have been affected by penetrating abdominopelvic trauma; therefore, understanding the reproductive issues in this population could have a significant impact on their quality of life.

The majority of studies in this review focused on direct trauma to reproductive organs although Janak et al. acknowledged that it is possible that some injuries to reproductive structures may go undetected in the immediate post injury period(18). Only one study explored the importance of counseling patients about their future reproductive potential. No studies provided a framework for a discussion and follow-up to address potential endocrine dysregulation and infertility that victims of gun violence may experience. There is a clear knowledge and process gap that needs to be filled around the impact of gun violence on future fertility.

This case report and scoping review have limitations. Case reports often discuss rare events which may not be widely applicable. Our case hopefully demonstrated the importance of understanding the possible intersections between gun violence and infertility. Moreover, scoping reviews may not comprehensively assess the available literature in the way that makes systematic reviews so valuable. Yet, scoping reviews have a role as a preliminary exploration of a topic when it is not clear what data exists around a specific subject matter.

The implementation of a scoping review in our study has some additional limitations. We used a narrowly defined set of search terms in order to precisely address our primary question. Other studies may have met criteria but were undetected if their titles and keywords did not fit with our search terms. As an example, we excluded studies centered on interpersonal violence and
sexual violence. Although these are important topics and may sometimes coincide with penetrating trauma, the subjects raised were often beyond the scope of this review. Additionally, only studies written in English with an easily accessible full text were included. It is possible that some valuable studies may have been excluded however in our review there were only six candidate studies without full-text available. Our investigational strategy models a comprehensive search that most English-speaking providers who might deal with civilian gun-violence might use.

Other medical issues that were not the subject of our primary objectives were raised in multiple sources for this review and deserve attention. Many of the case reports described a variable incidence of sexual dysfunction or hypogonadism (14)(15)(23). In addition to future fertility, sexual dysfunction was also a concern among veterans experiencing abdominopelvic trauma in the qualitative study from Lucas et al (23). Given the intersection between sexual dysfunction and infertility, including sexual dysfunction as a search term may have broadened our cohort of sources. However, the treatments for sexual dysfunction differ from infertility and because many of the etiologies for infertility are not as readily recognizable as sexual dysfunction, this scoping review focused on infertility.

Post-traumatic stress disorder (PTSD) was often co-diagnosed in trauma patients included in this review (19) (9)(18). Our findings are consistent with other work on surgical trauma and PTSD demonstrating that PTSD affects approximately 21% of people who survive their traumatic injuries(27). Importantly, there is a well-established connection between PTSD and sexual dysfunction (28). People with PTSD may also experience dysregulation of the hypothalamic pituitary axis, even in the absence of a direct traumatic brain injury (29). Just as the injuries to reproductive organs may occur concurrently with other trauma, the ways that these injuries influence fertility are inextricably related to endocrine concerns, mental health and functional abilities that may also impact future fertility. In addition, some people may self-medicate with marijuana to address PTSD symptoms however this can negatively impact semen parameters or potentially fertility (30).

This review demonstrates that there is increased interest in the epidemiology and management of penetrating abdominopelvic injuries such as gunshot wounds, with the majority of studies completed after 2000. Most of these injuries occur among people during the peak of their reproductive years. Furthermore, in the United States, African Americans are disproportionately affected by gun violence. The intersection of gun violence, race and fertility may represent a previously unrecognized contribution to infertility among people of color. Future studies on the prevalence of infertility among victims of gun violence may assist providers in understanding how to include this in their differential for patient seeking reproductive assistance.
Conclusion

In the United States, gun violence is a significant public health issue. Up to one in ten male trauma patients will experience urogenital trauma after a GSW. Despite the prevalence of abdominopelvic GSWs, there is a concerning paucity of data on the intersection these injuries and fertility. Furthermore, there is limited guidance on how to discuss issues of fertility with victims of gun violence who experience abdominopelvic trauma and the ideal follow-up regimen. A systematic framework to address penetrating trauma that may affect fertility has the potential to vastly improve fertility and potentially the quality of life for victims of gun violence who are often in the prime of their reproductive years.

Financial Support

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Acknowledgement We would like to thank Dr. Sam Ohlander for his commentary
References


Figure Legend

Table 2
*After treatment with pseudoephedrine and sodium bicarbonate; Post-ejaculate urine specimen with 1.9 M sperm and 36% motility
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<th>Table 1: Female Patient’s Relevant Labs and Evaluation</th>
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<td>Follicle stimulating hormone 11.2 IU/mL, estradiol level 37 pg/mL</td>
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<td>Thyroid Stimulating Hormone 0.54 mIU/L</td>
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<td>Anti-mullerian hormone level 1.25 ng/mL</td>
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<td>Saline sonohysterogram: Bilateral hydrosalpinges, left tubal patency, uterine cavity normal</td>
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Figure 1. PRISMA-Scoping Review Flow Diagram

Identification of studies via databases and registers

Records identified from*:
- Databases (n = 879)
- Registers (n = 0)

Records removed before screening:
- Duplicate records removed (n = 112)
- Records marked as ineligible by automation tools (n = 0)
- Records removed for other reasons (n = 0)

Records screened (n = 767)

Records excluded** (n = 718)

Reports sought for retrieval (n = 49)

Reports not retrieved (n = 6)

Reports assessed for eligibility (n = 43)

Reports excluded (n=18):
- Gunshots or penetrating trauma not included (n = 16)
- Study does not include humans (n = 1)
- Editorial (n = 1)

Studies included in review (n = 25)