Cost analysis of a Fracture Liaison Service: a prospective randomized study for secondary prevention after fragility fractures of the hip

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Abstract

**Background:** Fracture liaison services (FLS) have proven to be effective in treating osteoporosis associated with fragility fractures. For patients with fragility fractures of the hip, FLS programs are expected to be cost-effective because of the high risk of re-fracture and the high cost of fracture treatment. In this study we evaluate the essential factors in determining whether the FLS saves or loses more than it costs.

**Methods:** A prospective-randomized study was done in patients with hip fragility fractures using a hospital-based FLS program in parallel with a cost analysis. Data was generated from a cohort of patients using actual data for FLS effectiveness, individual costs of hip fracture treatment, and medication costs based on an accepted treatment algorithm.

**Results:** There were 200 patients randomized and 180 analyzed for costs. Results showed that the cost-benefit of the FLS was dependent on the medication used for osteoporosis. Specifically, using the medication algorithm in this study, the loss per patient enrolled in the FLS was $671 for a 2-year period. If intravenous zoledronic acid had been used, then the loss would have been $221. If only oral bisphosphonates had been used, then the FLS would have saved $109 per patient for a 2-year period.

**Conclusions:** The analysis done here shows that medication cost is the critical component in cost-effectiveness of a FLS program. Additional work needs to be done refining the medication algorithm considering medication costs but individualized to patient needs based on fracture risk.

**Trial Registration:** NCT02239523

Background

Osteoporosis is a worldwide epidemic. Despite well-known protocols, less than 15% of patients get treated for underlying osteoporosis after a hip fracture\(^1\). For those who sustain a fragility fracture, the risk of a subsequent fracture is 2-4 times higher\(^2,3\). Strategies to improve compliance with recommended standards have generally not been effective\(^4\). The exceptions are those programs with a fracture liaison service (FLS) with a dedicated team\(^5\). FLS programs appear to be the best and potentially the only reliable method to get patients started on osteoporosis treatment. The challenge then is who is willing to pay?

The purpose of this study is to better understand the factors that influence the costs and potential savings of a FLS program. Patients who suffer a hip fragility fracture are at a high risk for secondary fragility fractures. This high risk of re-fracture along with the high cost of treating additional fractures makes this post hip fracture group uniquely suited as a focus for secondary prevention. The costs of a secondary prevention program may be offset by the savings of preventing future expected fragility fractures. The International Osteoporosis Foundation (IOF) recommends that programs interested in
starting a FLS program should start with secondary prevention of hip fractures for precisely these reasons.

We performed a prospective randomized study with a dual purpose of improving compliance with starting osteoporosis medication after hip fragility fractures in parallel with an analysis of the costs incurred for treating these fractures. Specifically, we calculated the actual costs of hip fracture treatment for each patient individually. Using these calculated costs with the actual effectiveness and costs of our FLS, we were able to accurately estimate the costs and savings of having a secondary FLS program. The objective of this study is to elucidate the factors that can make a secondary FLS program either profitable or a burden to a system. In addition, we evaluated the costs and savings separately from the perspective of the hospital and the insurance system to determine whether a FLS would be beneficial for one or the other.

Methods

Inclusion/Exclusion Criteria:

This study was conducted in compliance with the ethical standards of the hospital on human subjects as well as with the Helsinki Declaration. All patients over the age of 50 admitted to our institution with a fragility-related hip fracture were considered for inclusion. A fragility fracture is defined here as a fracture resulting from a low energy fall typically occurring while standing or walking. Exclusion criteria included patients with a fracture sustained in a non-low energy fall, those with metastatic cancer or known metabolic bone disease or patients in end-of-life care. Patients unable to undergo consent because of dementia were excluded, but if their dementia was mild and consent could be obtained, they were included.

Randomization:

All patients that met the study criteria gave written informed consent before randomization. The patients were prospectively randomized equally into one of two levels of intervention (see below). The statistician used a random number generator for one of two options (Group A or B) using 2 blocks of 100. The sequence was not concealed from the research assistant who enrolled the patients into the study. The study was not blinded for the intervention.

Intervention:

The control group received a letter at time of discharge encouraging their primary care physician to start medication for osteoporosis. The intervention group had four interventions including printed information about osteoporosis, a DEXA scan, a specific treatment recommendation (Figure 1) to give to their primary care physician to initiate treatment, and monthly phone calls from the study coordinator for 4 months.

Treatment Algorithm (Figure 1):
The treatment algorithm was designed to guide primary care physicians on medication treatment for secondary prevention. It was designed to give them 2 options for each of 3 patient scenarios. The default treatment recommendation was intravenous bisphosphonates based on the success of the Horizon study\(^6\) and reduced need for patient compliance compared to weekly oral bisphosphonates. Denosumab was an option for patients who were considered “treatment failures” if they had a fragility fracture while on bisphosphonates for 2 years or more. Other reasons for recommending denosumab included patients who had renal failure, declined intravenous zoledronic acid because of previous experience or concern about flu-like symptoms. Teriparatide was an option for patients who were treatment failures on bisphosphonates or had a higher risk of additional secondary fractures based on the individual patient profile that included DEXA and FRAX scores.

**Savings of the FLS program:**

The savings of an FLS program is the amount saved by reducing the costs of having to treat future secondary fractures. There are three related components. The first component is the effectiveness of an FLS program in getting patients on recommended treatment. The second component is the effectiveness of that treatment. That is, how much will appropriate treatment reduce the frequency of secondary fractures compared to no treatment. The third component is the costs and frequency of the different types of additional fragility fractures. Then, knowing the costs of treating secondary fractures, and knowing the reduction in these fractures, the amount saved can be calculated.

For example, if treating a hip fracture cost $100 and there are normally 20 fractures in a 2-year period then costs would be $2000 over 2 years treating hip fractures. If the FLS program reduces these fractures by 10% compared to no treatment, then the savings would be $200 over 2 years. However, if only 50% of patients enrolled in the FLS program and started the medication, then the savings would be $100 over 2 years. One could then compare this to the costs of an FLS program to determine if money was overall saved or lost.

**Costs of fragility fracture treatment:**

For the cost of treating hip fractures, we used our prospective data calculated for this study. For other fragility fractures such as spine, and distal radius or proximal humerus (non-hip and non-vertebral), we calculated the costs for the type of fracture including an estimate of how often they are treated conservatively versus surgically and the different costs for treatment (Appendix 1).

**Hospital Perspective for Hip Fracture Care**

The costs and reimbursement to each patient hospitalized for hip fractures were individually calculated and a detailed analysis was performed. The costs for hip fracture care were impacted by many factors including for example preoperative evaluation, the type of implant and the length of hospitalization. Costs related to complications or re-admission within 30 days was an important part of the analysis.
Costs to the System for secondary fracture treatment:

The Horizon study\(^6\) evaluated the effectiveness in reduction of secondary fractures for three categories including hip, vertebral and non-hip/non-vertebral. The costs for hip fracture treatment were directly calculated as described above. The costs and frequency for vertebral and non-hip/non-vertebral based were estimated based on historical data (Appendix 1).

Expected reduction in re-fractures based on Horizon study:

To determine the effectiveness of a FLS program on reducing fracture incidence, we used information from the Horizon study\(^6\). That industry-sponsored study was prospective, well-powered with nearly 2-year follow-up. They used intravenous bisphosphonates that eliminated the issue of compliance. They found refracture rates (of secondary fractures) for those on treatment compared to those not on treatment of 8.6\% versus 13.9\% respectively. We used their reduced re-fracture rate along with our FLS effectiveness rate to calculate the savings per patient for each of the three categories of fractures, hip, vertebral and non-hip/non-vertebral (available upon request).

Costs of the FLS program:

The costs of an FLS have 3 primary components: the cost of the program coordinator and overhead, the costs of additional laboratory (and DEXA) evaluation and the costs for the medications that the patients take for osteoporosis treatment. The total of these costs was then averaged to provide the cost for FLS care per patient over a 2-year period. Labs that are routinely done on admission for hip fracture care were not considered an added cost for an FLS since they would be needed in any case for preoperative evaluation. Other labs that were indicated based on the FLS program algorithm and not routine were added as FLS costs. For example, PTH (parathyroid hormone) levels had specific indications (Calcium level more than 10.5 mg/dL) and this lab when indicated, was included as an added cost. Although the dual-energy X-ray absorptiometry (DEXA) scan is not required to initiate treatment since a fragility fracture is determined by the mechanism of low energy, DEXA scan is generally recommended and often useful. One advantage of having a baseline DEXA is to follow effectiveness of treatment. Another advantage was in identifying patients with unusually low bone densities that are at higher risk and therefore warrant treatment with more effective and expensive medications\(^7\).

Results

The enrollment period was from February 21, 2017, to September 15, 2018 when 200 patients were reached. This number was chosen based on a power calculation used for the intervention part of the study\(^8\). Since there is no control group for the cost analysis, no a priori power calculation was needed. During the enrollment period, there were 618 low-energy hip fractures of which 305 were eligible for enrollment (see flow diagram Figure 2). Most of the patients not eligible were excluded due to moderate or severe dementia, an exclusion criterion for this study. Sixty-six percent of those eligible agreed to participate in the study.
Baseline characteristics were not different between groups (Table 1). The age range was 51 to 95 years with an average age of 79.2 (± 9.2) years. Seventy-two percent were female. Of the 100 patients randomized to each group, 97 were analyzed in the letter group and 83 in the intervention group.

(Table 1 here)

Patients were hospitalized an average of 11.7 days (S.D. 14.6) with range of 3 to 133 days (median 8.0 days). This included complications both medical and surgical that resulted in prolonged hospitalizations.

Preoperative hip imaging (in addition to plain x-rays) was done in 19 patients including 17 that required a CT scan and 2 that required an MRI to confirm non-displaced fractures after plain x-rays could not confirm the diagnosis. Preoperative imaging was also done for medical reasons including echocardiogram in 14 and head CT in 18.

Hip implants included cannulated screws in 25 (12.5%), gamma nail 97 (48.5%), bipolar 38 (19%), THA (total hip arthroplasty) 3 (1.5%), PF2 (Zimmer implant) 16 (8%), PCCP (percutaneous compression plating) 13 (6.5%), PFNA (proximal femoral nail anti-rotation) 5 (2.5%), and no surgery in 3 (1.5%).

Complications:

Overall, there were 40 patients (20%) with complications including 12 (6%) with surgical complications, 22 (11%) with medical complications and 6 (3%) with both surgical and medical complications.

Surgical complications included deep wound infection (7), superficial wound infection (3), hardware failure (4) and artery perforation or pseudoaneurysm requiring interventional radiology coiling (2).

Medical complications (some with more than one complication in a patient) included pulmonary embolism (1), urinary tract infection (5), renal failure (12), stroke (1), heart failure exacerbation (12), pneumonia (7), other (6) including gallstones, atrial fibrillation, GI bleed, intra-cranial bleed, terminal ileitis, general deterioration, and death (6).

Hospital Perspective - cost of treating hip fracture:

The average cost per patient of treating a hip fracture for the hospital (including complications) averaged $14,200 (SD $12,850 and range from $2770 to $109,700) (Figure 3).

Health insurance reimbursement was an average of $10,070 (SD $8157 and range from $1999 to $76,220) leaving an average loss for the hospital of $4132 (S.D. $5789 with range of loss of $33,520 to profit of $5873) per hip fracture.

Net gain or loss in NIS (Israeli Shekels) for each patient (Costs in Israeli Shekels were converted to US Dollars at the average 2019 rate of 1 USD = 3.5645 Shekel from www.boi.org.il):

National Health Insurance Perspective-- cost of treating hip fracture:
The average payment from the health insurance to the hospital was $10,070 per hip fracture. Rehabilitation adds approximately $4619 bringing the total average cost per hip fracture for the health insurance to $14,670.

Costs to the System for hip fracture treatment:

The cost to the system includes the combined loss to both the hospital and the health insurance. In otherwords, the system lost an average of $18,800 per patient for the care of a hip fracture. These costs would represent the potential savings to the health care system of an effective FLS program based on how many of these hip fractures would be prevented for a two-year period.

Expected reduction in hip re-fractures based on our FLS effectiveness:

In the first part of this prospective study, we enrolled 200 patients equally into 2 groups to determined effectiveness of our FLS program. At 4 months from the fracture, the rate of patients on recommended treatment was determined for each group. The rate of treatment for the Letter group at 4 months was only 6% compared to the Intervention group with 77% [8]. We used this enrollment rate for the purpose of calculations in this cost analysis for effectiveness of our FLS program.

Medication costs (Appendix 2):

The cost of medications had the greatest impact on cost of FLS care. The Israel Ministry of Health is mandated by law to require the health insurance to pay for most of the costs of medications including bisphosphonates, but coverage also includes the more expensive options such as teriparatide or denosumab after a hip fracture. For other types of fragility-related fractures, such as wrist or spine, the more expensive options are not covered unless approved by an endocrinologist. Therefore, the calculations and cost-benefit analysis determined here would be different if the initial fracture was not a hip fracture or if we used a different algorithm for choosing medications (more in the Discussion section).

Most patients were started on either zoledronic acid or denosumab. There were some patients that were started on teriparatide and 2 other medications (available upon request). The costs of medications were calculated for each patient then averaged for the group (available upon request).

Expected Savings from FLS Program (Appendix 3):

Cost-Benefit Ratio for a hospital-based FLS program:

The FLS we started was orthopedic-inspired and based in the hospital. Using the non-medication FLS cost of $172 and expected per patient savings and for reducing future fractures of $30, we calculated an overall projected loss per patient of $142 over 2 years. Since medications were not a factor for the hospital, this loss did not affect the hospital cost-benefit ratio.

Cost-Benefit Ratio for a health insurance-based FLS program:
Here we assume that the FLS would be managed by the insurance provider. Using the average per patient FLS cost (over 2 years) of $1250 (that includes medication) and savings of $579 (for reduced cost of treating secondary fractures) we calculate an overall loss of $671 per patient per 2 years. It is important to note that costs calculated here include the FLS program, the DEXA scans and the medications. The medications were the bulk of the cost at $1078 (86% of the costs).

If patients had all been given zoledronic acid then the FLS medication costs would have been reduced to $628 and total costs reduced to $800 giving a loss of $221 per patient for 2 years. If generic oral bisphosphonates (Alendronate once weekly) had been given, the medication cost would have been $298 or a total cost of $470 giving a profit for the FLS program of $109 per patient for 2 years.

**Discussion**

When this study was started, it was assumed that the amount saved would be more than enough to pay for the program. After all, hip fracture treatment is expensive, and the salary of a nurse coordinator is relatively low. Our initial back-of-the-napkin analysis estimated the cost of a ½ time nurse coordinator (for our volume of hip fractures) at $30,000 per year, and with the hospital loss of $4132 for each hip fracture, it would take reducing only 7.3 hip fractures per year for a hospital based FLS program to pay for itself. In our institution, we treat over 600 hip fractures per year and with only 1% reduction in secondary fractures, having 6 less hip fractures is possible. For the national insurance, starting a FLS program is even more favorable. With loss of $14,670 per hip fracture, it would take reducing only 1 hip fracture per year to pay the part-time coordinator salary. Indeed, Majumdar et al.\(^9\) used exactly this type of analysis and concluded that their FLS program only costs $50 per patient. They assumed a FLS coordinator salary of $33.3/hr with 30% overhead and we used $34/hr and 20% overhead. However, the actual costs of a FLS program are more complex.

**Overall Savings:**

Cooper et al.\(^{10}\) used a Markov model in the Canadian system using different assumptions to calculate an average savings of $88 per patient over 10 years (with range from -$379 to $693 (ratio of 1 AUD = 0.76 USD). Their FLS used bisphosphonates for post-fracture treatment. Solomon et al.\(^{11}\) did a cost-effectiveness analysis of a FLS program after a hip fracture in the US health care system using a Markov computer simulation model. They concluded that an FLS program would reduce hip fractures by 1.1% which is comparable to the 1.11% used in this study. They showed a cost savings of their post-fracture FLS of $6.68 per patient. Their model used fracture reduction rates using bisphosphonate therapy from previously published data.

McLellan\(^{12}\) did an elegant cost-effectiveness analysis using 8 years of data from the West Glasgow FLS. For a hypothetical cohort of 1000 fragility fracture patients, they estimated a reduction of 11 secondary hip fractures (1.1%) and an additional 7 (0.7%) non-hip fractures saving £21,000 or approximately $28.2 per patient enrolled. They used bisphosphonates in 55% of the patients and Ca/Vit D only in 40%.
Our study strengths include real-life data rather than primarily estimates. For example, in determining cost of hip fracture care, the cost for each patient was individually calculated that included factors such as length of stay and complications. The actual effectiveness of our program was determined prospectively and perhaps most important, the medication costs were based on actual patient data.

Our study had several limitations. We did not include patients with moderate or severe dementia. This was because the study requires consent, and the intervention program required the patient to be in contact monthly. Another limitation of the study is that our system recognizes complications related to the initial procedure only up to 30 days. If the patient was re-admitted after that time, but was still related to the index procedure, it would not have been counted and therefore costs might be underestimated. The two-year horizon used for this analysis was chosen since the Horizon study\textsuperscript{6} had the best data for fracture reduction. This study was not designed to prospectively follow individual patients. In addition, medication costs over a longer time frame would presumably be more effective at reducing secondary fractures but would also significantly increase costs. We believe that the conclusions of this study would remain unchanged that medication costs are the critical factor in profitability of a FLS program.

The greatest argument might be that our medication algorithm was not appropriate. Patients with a higher risk of re-fracture based on their combined FRAX scores and DEXA scans might benefit from the more effective and expensive options whereas most of the patients may only need bisphosphonates\textsuperscript{13}. Before starting the study, we met with the endocrinologists that advise each of the four different national health insurance programs in Israel and all agreed with the proposed algorithm. Importantly, all the medications are part of the American Association of Clinical Endocrinologists (AACE) and American College of Endocrinology (ACE) clinical practice guidelines for osteoporosis treatment\textsuperscript{14}. The Israel Ministry of Health has approved all the medications for treatment after hip fractures given the unique risk in this group of patients.

We believe that the analysis here is not unique to the Israel health care system. The components of the analysis and the relative costs of the components should be comparable within other health care systems. We hope the information provided in this analysis can help the interested physician advocate or insurance provider design an effective and cost-efficient FLS for an increasingly elderly population. Everyone loses with low energy hip fractures: patients, hospitals, and the national health care system. The solution is to invest properly in a well-designed FLS program.

Conclusions

The analysis done here shows that medication cost is the critical component in cost-effectiveness of a FLS program. Additional work needs to be done refining the medication algorithm considering medication costs but individualized to patient needs based on fracture risk.

Declarations
Ethics approval and consent to participate: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. All patients that met the study criteria gave written informed consent before randomization. Clinical Trials Number: 201497CTIL (first posted 12.09.2014 https://clinicaltrials.gov/ct2/show/NCT02239523?term=201497CTIL&draw=2&rank=1). This study was approved by the Helsinki Committee at Shaare Zedek Medical Center, Jerusalem.

Consent for publication: Not applicable.

Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors: GZ, AD, NS, YL and AP declare that they have no competing interests.

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Authors’ contributions: GS was responsible for concept and execution of the study and drafting and revision of the manuscript. AD was responsible for data management of the costs for the hip fractures including setting up and collecting the data and analysis. NS was responsible for providing endocrine guidance including the protocol and treatment regarding individual patients. YL was responsible for intellectual content and manuscript drafts. AP was responsible for overall project guidance and manuscript drafts.

Acknowledgements: None

References


Table

Table 1: Baseline characteristics of Letter versus Intervention groups
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**Figures**
Treatment Recommendation for Osteoporosis/Osteopenia

Regarding: Name ________________________  ID____________________

Dear Doctor, your patient has sustained a fracture of the hip as a result of underlying osteopenia or osteoporosis. Recommendations based on best-practice are for the patient to be on medication to help prevent additional future fragility-related fractures.

The recommended treatment listed below is based on the specific medical history of the patient named above. Please note that the recommendations are based on published data and approved by the Ministry of Health and reviewed by a specialist in each of the kupot (Clalit, Leumit, Macabbi, Meuchedet)

We recommend the following for ALL patients:

☐ Vitamin D 1000 IU/day  OR if pt has renal failure  ☐ Alpha D3 0.25 micrograms/day

and  ☐ Calcium 600 mg/day

The last calcium level: _____ The last albumin level: _____ Date of labs: ______

Your patient’s adjusted calcium level* is: ______ mg/dL (normal range is 8.5-10.2 mg/dL)

*[Adjusted Calcium Level= Total Calcium + 0.8 x (4.0 – Albumin Level)] mg/dL

Please order the following medication (after adjusted calcium > 8.5mg/dL):

☐ Not initially on medication (not on bisphosphonate or on bisphosphonate < 12 months):

1. Aclasta (zoledronic acid) - intravenously once yearly (5mg) – (preferred treatment).

2. Prolia (denosumab) – subcutaneous injection of 60 mg every 6 months (second line option).

☐ Someone who had hip fracture while on bisphosphonate Tx ≥ (12 months) - considered treatment failure:

1. Forteo (teriparatide) - 20 micrograms subcutaneously once a day (for 2 years) - (preferred treatment).

2. Prolia (denosumab) - subcutaneous injection of 60 mg every 6 months (second line option).

☐ Renal failure (creatinine clearance <30 mL/min)

Prolia (only option) – subcutaneous injection of 50 mg every 6 months, (relative contraindication is active auto-immune disease).

- In Rheumatology and Autoimmune diseases (like SLE) should be careful in giving Prolia.

Figure 1

Recommendation algorithm for osteoporosis treatment
Figure 2

Hip fractures flow diagram
Figure 3

Net gain or loss in treatment per individual patient (in NIS)

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Supplemental1Averagesavingsforreducedfractures.docx
- Supplemental2Costsforfractures.docx
- Supplemental3MedicationPrices.docx