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Assessing Risk of Non-Fatal Outcomes Amid a Competing Risk of Mortality: The Example of Hip Fracture

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Abstract

Background: Factors like age, sex, and race are associated with risk of hip fracture but also with mortality. Substantial misunderstanding remains regarding the appropriate statistical approach to account for the competing risk of mortality.

Methods: In the Cardiovascular Health Study, an ongoing cohort study of 5,888 older adults, we followed participants for incident hip fracture from their 1992–1993 visit through June 2014. We contrasted the conventional cause-specific Cox analysis, which censors individuals at the time of death, with the Fine-Gray (FG) approach, which extends participant follow-up even after death, to estimate the association of well-established demographic and clinical factors with incident hip fracture.

Results: For age, current smoking and sex, Cox and FG methods yielded directionally concordant but quantitatively different strengths of association. For example, the Cox hazard ratio (HR) for a 5-year increment in age was 1.74 (95% CI, 1.61–1.87), while the corresponding FG HR was 1.16 (1.09–1.24). In contrast, the FG approach estimated a stronger association of hip fracture with sex. The two approaches yielded nearly identical results for race. For diabetes and kidney function the estimates were discordant in direction and the FG HRs suggested the opposite direction of well-understood and widely-accepted associations.

Conclusions: Cause-specific Cox models provide appropriate estimates of risk for non-fatal outcomes like hip fracture even in the presence of competing risk of mortality. The Cox approach estimates risk in the population of individuals who have not yet had an incident hip fracture and remain alive, which is typically the group of clinical interest. Fine-Gray method estimates risk in a purely hypothetical population that can yield misleading inferences about populations of clinical interest.

Keywords

competing risk; mortality; hip fracture; Fine-Gray approach; Cox regression

Introduction & Methodology

In geriatric research, mortality often precludes individuals from reaching the end of clinical follow-up. Death makes it impossible to experience and observe the primary event of interest. Other common occurrences in geriatric populations, such as institutionalization, may also have the effect of limiting observation of the primary event. Many statisticians and non-statisticians believe that accounting for death by censoring future follow-up years results in biased findings [1]. Perhaps the most widely used alternative method to conventional regression censoring individuals at the time of death is the Fine-Gray (FG) approach [2]. Substantial confusion exists about this methodology [3, 4, and 5]. A systematic review of the use and interpretation of the FG methodology in 2015 found that only 9% of papers in which the method was used interpreted FG estimates correctly [3]. Nonetheless, researchers continue to use the FG methodology for studies of risk factors in the geriatric literature in general and for hip fracture in particular [6, 7, 8, 9].

To understand the difference between these methods, a brief review of survival analysis is useful. In time to event data, the outcome of interest is not only whether or not an event occurred, but also the time at which the event occurred. Censoring occurs when an individual is lost to follow-up before experiencing the event and before the end of the study. In that situation, inferences from the observed, partially censored population can only be generalized in an unbiased manner to the entire population if censoring is non-informative [10]. That is, individuals who remain under follow-up are similar to those who were censored. Competing risk is a form of censoring, when we observe only the first of the primary and a competing event. Death is a model example of competing risk for it necessarily precludes observation of any subsequent events.

Two populations can be conceived in the presence of competing risk of death. In one, a largely hypothetical population, death does not preclude an individual from experiencing the primary event, but merely precludes its observation. In other words, one wishes to know when a primary event would have happened had not the person died. The FG approach operates in this population, wherein individuals with competing events (including death) remain in the population at risk until the end of study despite having no risk of hip fracture. In essence, the competing event of death protects them from ever sustaining a hip fracture, not only from observing it. The sub distribution hazard from FG [5] therefore estimates the instantaneous rate of incident hip fracture among individuals who are currently alive and free of incident hip-fracture as well as those who have died but remain ‘observable’ until the end of the study. Those subjects who have died prior to sustaining a hip fracture are artificially retained in the risk set. The FG approach estimates a hazard in the entire population regardless of whether an individual is truly at risk of incident hip fracture or is not.

In contrast, the more commonly conceived, and more intuitively useful population, is comprised of all individuals alive up to any given point during follow-up, for whom one is interested in their subsequent risk. This approach is called cause-specific (CS); CS Cox regression is the most common form [11]. In that setting, importantly, this approach does not exclude individuals who die during follow-up, but merely censors them at the time of their

death; that is, it incorporates all of their observable person-time while alive. In the conventional CS Cox regression [11], the instantaneous rate of incident hip fracture among individuals who are still alive is modeled – a useful parameter clinically. Even though CS Cox regression is often not considered a “competing risk” approach, it is nonetheless a valid approach contrasting individuals who are truly at risk across different levels of risk factors even in the presence of competing risk.

As previously noted, the FG approach assumes that hip fractures can, but do not, occur after the competing event; that is, once the competing event occurs, subjects become ‘immune’ to the primary event. An intuitively opposite approach would be to treat each competing event as a primary event. Thus, one could model a “composite event” of hip fracture and death. This approach has a ready interpretation, for it models the instantaneous rate of a single event among everyone at risk. However, drawing clinical inferences from a composite outcome model is challenging due to heterogeneity of its components [12, 13]. Importantly, however, the FG approach and the composite outcome approach represent lower and upper boundaries to the true rate of events, respectively (i.e., because follow-up continues after the competing event with no new primary events in FG, while follow-up ceases with the maximum number of primary events with the composite event approach). For a contrast measure such as hazard ratios there is no such implication.

Importantly, the FG approach uses the same underlying model and statistical equations for estimating hazard ratios, as does the traditional CS Cox approach [5]. By redefining the population at risk, FG redefines the hazard function, known as a sub distribution hazard. For ease of communication, we use the term FG when referring to estimating the sub distribution hazard using Cox statistical methodology and we reserve the term Cox approach for estimating the CS hazard with Cox regression.

In the following sections, we contrast the conventional CS Cox approach, the Fine-Gray approach that is often used and recommended, and the composite event approach. We demonstrate their impact using the Cardiovascular Health Study (CHS), examining hip fracture as the primary outcome and mortality as the competing event. We use a selected series of well-understood risk factors to illustrate how these approaches differ. Our results highlight how the two approaches may come to different conclusions and emphasize the credibility of the Cox approach even in the presence of competing risk.

Methods

Participants

The CHS is a prospective, population-based cohort study of 5,888 Medicare-eligible adults of at least 65 years of age in four US communities [14]. In the original cohort, 5,201 eligible men and women were enrolled during 1989–1990. In the second recruitment, during 1992–1993, an additional 687 predominantly black men and women were enrolled. All participants signed informed consent upon study entry. CHS prospectively gathers all hospitalization data, including discharge summaries, from participants every six months.

Outcome

Incident hip fracture was identified using International Classification of Diseases, Ninth Revision (ICD-9) codes from hospitalization records from the time of the 1992–1993 visit through June 30, 2014. Hip fracture was defined as ICD-9 code of 820.xx. Admissions for pathological fractures (ICD-9 code 773.1x) and motor vehicle accidents (E810.xx-E825.xx) were not considered as hip fractures.

Risk factors

For this illustrative example, we used six common risk factors for hip fracture – age, sex, race, smoking, kidney function, and diabetes. All have been associated with risk of hip fracture in younger populations in which competing risk is less substantial [15–19]. Smoking history was obtained by participant self-report. Renal function was assessed by cystatin C-based estimated glomerular filtration rate. Diabetes was defined as use of insulin or oral hypoglycemic agents, or fasting glucose level ≥ 126 mg/dL.

Statistical Methods

In all models, we used Cox regression to estimate hazard ratios. The only difference between the cause-specific approach and the Fine-Gray methodology is the manner in which individuals who died are coded at the time of death and thereafter. With the CS approach, we modeled the hazard among individuals alive up to the point of death. With FG, we modeled the sub-distribution hazard [2], a hazard in the entire population where anyone who dies is ‘immune’ to hip fracture until the end of the study, regardless of risk factor profile.

We first created a model with age, gender and race (model 1). We then added well-established risk factors into model 1 and ran separate regressions for each risk factor. The risk factors are current smoking, cystatin C-based eGFR (per 15 mL/min/1.73 m²), and diabetes status.

All statistical analysis was conducted in R [20].

Results

Among 5265 participants followed for a median of 11 years (inter-quartile range 6–17, maximum 22), 688 incident hip fractures occurred. In addition, 3979 individuals (76%) died prior to incident hip fracture, representing the competing risk. Another 601 participants died following hip fracture, leaving 598 individuals who reached the end of follow-up without any event. Table 1 presents selected baseline characteristics of the study population. The average age at baseline was 75 years, 59% were women, 17% were black, and 10% were current smokers. Prevalence of diabetes was 17%, and the average eGFR was 73 mL/min/1.73 m².

Table 2 presents results of models that include standard demographic factors of age, gender, and race. The Cox HR for incident hip fracture associated with a 5-year higher age was 1.74 (95% CI 1.61, 1.87). The corresponding FG sub distribution hazard ratio estimate was 1.16 (95% CI 1.09, 1.24). This estimate implies an effect of age that is almost five times lower

than the Cox estimate, which assesses risk only among those alive at any given point. Death itself is positively associated with age. By setting the risk for hip fracture to zero among those who died, the FG approach lowers the apparent importance of age. This attenuation is particularly dramatic because the proportion of individuals who died during follow-up is large and the association of death with age is strong. The hazard ratio for a composite endpoint of hip fracture and death was similar to the hazard ratio for mortality alone because the composite event is dominated by mortality. This is the case for hazard ratios of all risk factors.

The association of incident hip fracture with sex demonstrates that FG approach can also yield estimates further from the null. The Cox HR estimate for male versus female sex is 0.62 (95% CI 0.53, 0.74), while the FG sub distribution hazard ratio estimate is 0.49 (95% CI 0.41, 0.58). In this case, the explanation is the opposite direction of the association between male sex and death (positive) and that of male sex and hip fracture (inverse). Since mortality is similar among whites and blacks, the HRs for race estimated by the two methods did not differ.

The two regression approaches can sometimes lead to qualitative differences as well, as demonstrated in Table 3. The Cox method suggests the expected association between incident hip fracture and current smoking (HR 1.66 (95% CI 1.28, 2.14)). In contrast, the FG approach suggests no statistically significant association. Because current smoking is associated with mortality, the FG approach tends to dilute the hazard ratio for current smoking.

Last, the Cox and FG approaches may come to opposite conclusions. For example, while we do not find a statistically significant association between higher cystatin C-based eGFR and risk of hip fracture (HR 0.95, 95% CI 0.89, 1.02) using the Cox approach, the association was inverse, as expected. In contrast, the FG approach finds an implausible harmful association associated with higher eGFR (HR 1.09, 95% CI 1.02, 1.17, $p < 0.01$).

The association of diabetes with risk of hip fracture also appears implausible in the FG approach. In Cox analyses, there is a non-significant association toward higher risk associated with diabetes (HR 1.19, 95% CI 0.94, 1.52), but the FG approach suggests a protective trend (HR 0.79, 95% CI 0.62, 1.01, $p=0.06$).

Discussion

CHS has proven to be a rich source of information on risk factors for hip fracture, but also illustrates the differences in methods addressing competing risk extremely well owing to its prolonged follow up and the large proportion of the cohort that is now deceased. In this setting, we demonstrated sharp differences between traditional Cox and Fine-Gray methods that highlight the value of standard methodology even in the presence of extreme degrees of competing risk.

The traditional Cox regression association contrasting current smoking with non-smoking on risk of hip fracture that we estimated here is consistent with a substantial external body of evidence. For example, a recent meta-analysis of 14 prospective cohort studies in men

estimated this association with a relative risk (RR) of 1.47 (95% CI 1.28, 1.66) [15]. In women, a meta-analysis of 10 prospective cohort studies estimated the contrast between current smokers and current non-smokers to be RR of 1.54 (95% CI 1.20, 1.87) [16]. A different meta-analysis in both men and women, adjusting for race, age, and gender, found an even higher RR of 1.84 (95% CI 1.52, 2.22) [17]. Our results using traditional Cox regression match these results extremely well, despite the lesser degrees of competing risk seen in younger cohorts with shorter follow-up.

In the Atherosclerosis Risk in Communities (ARIC) study of middle-aged individuals, where the competing risk of death is smaller than in older adults, a negative association was found between cysGFR and risk of hip fracture that had a similar magnitude to the estimated HR found in CHS data with traditional Cox. An opposite direction of association was found with the Fine-Gray approach [18]. Similarly, and contrary to the Fine-Gray approach finding in CHS regarding diabetes, ARIC investigators found diabetes to increase risk of fracture-related hospitalization [19]. Their sensitivity analysis using the Fine-Gray approach found the positive association attenuated by half, but still significant. In CHS, where the majority of the population died before experiencing a hip fracture or reaching the end of the study (76%), the protective effect of death in the Fine-Gray approach not only attenuated the risk but paradoxically reversed the association into diabetes being protective against hip fracture. The composite event approach in all risk factors provided estimates similar to the mortality estimates, because over 85% of the composite events were deaths.

In general, the Fine-Gray methodology is not intended for etiologic questions [4, 12]. The Fine-Gray approach was not specifically designed to solve problems with competing risk, but rather to estimate sub distribution hazard ratios that would more closely correspond to cumulative incidence ratios from the entire population than do standard hazard ratios among individuals at risk. However, this correspondence does nothing to improve the ability of its method to answer questions about risk factors, and several of the examples here illustrate why.

In spite of the popular belief that the FG approach answers the question about what would have happened had the competing event not occurred, which is clearly a question of great interest, it in fact does not accomplish that. The FG approach adds more time at risk – following death, in the case described here – but NOT more events. Thus, the competing event, death in our scenario, protects individuals from the occurrence of the primary event. The question of what would have happened had the competing event not occurred naturally presumes that some cases would have accrued had participants not been censored, but the FG approach unrealistically presumes the opposite. In contrast, when modeling the hazard of a composite event, we add no additional time at risk but all the competing events. Taking the opposite standpoint to the FG approach, the competing event, death in our scenario, is considered an event. The heterogeneity of the primary and competing event and the amount of competing risk in the population drive the inference of the composite event approach.

When estimating hazard ratios for association of an event and a predictor, the conventional Cox approach estimates the hazard of the event in individuals who are event-free and alive – the group of individuals a clinician faces when implementing its results. The FG approach

dilutes that association, attenuating the magnitude of HRs, if the predictor influences risk of both the primary and competing outcomes in the same direction. Similarly, the FG approach overestimates the magnitude of the association in individuals at risk if the effect is opposite for the two types of events. In neither case, however, does the FG approach necessarily better estimate what would have happened in the absence of competing risk.

Although the Fine-Gray approach was introduced almost 20 years ago, and its developers have themselves cautioned about its misuse, clinical researchers continue to misinterpret its output, particularly in fields such as geriatrics where competing events are common. In our view, recognition of how individuals who experience the competing event are accommodated in the two approaches clarifies the problems that can accompany the use and interpretation of the Fine-Gray approach. As the examples here illustrate, the FG approach can yield estimates close to or far from those of traditional CS Cox analysis and that are closer to or further from the null. They can also produce results that contradict well-established associations observed in cohorts much less susceptible to competing risk. In our view, FG should be used for its original intention – namely to yield adjusted estimates of hazard ratios that are indirectly related to the cumulative incidence ratios in entire samples or in specific subgroups – but traditional CS Cox analysis, which has served survival analyses for decades, should continue to be used when questions about association of outcomes in clinical subsets at risk are addressed, even in the presence of competing risk.

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References

- [1]. Berry S, Ngo L, Samelson EJ, Kiel D. Competing Risk of Death: An Important Consideration in Studies of Older Adults. *J Am Geriatr Soc* 2010 58(4):783–787. [PubMed: 20345862]
- [2]. Fine JP, Gray RJ. A Proportional Hazards Model for the Subdistribution of a Competing Risk. *J Am Statistical Association*. 1999 94(446):496–509.
- [3]. Austin PC, Fine JP. Practical Recommendations for reporting Fine-Gray Model Analyses for Competing Risk Data. *Statistics in Medicine*. 2017 36:4391–4400. [PubMed: 28913837]
- [4]. Austin PC, Lee DS, Fine JP. Introduction to the Analysis of Survival Data in the Presence of Competing Risks. *Circulation*. 2016 83:311–321.
- [5]. Latouche A, Allignol A, Beyersmann J, Labopin M, Fine JP. A competing risks analysis should report results on all cause-specific hazards and cumulative incidence functions. *Journal of Clinical Epidemiology*. 2013 66(6):648–653. [PubMed: 23415868]
- [6]. Szulc P, Blackwell T, Kiel DP, Schousboe JP, Cauley J, Hillier T, et al. Abdominal aortic calcification and risk of fracture among older women the SOF study. *Bone*. 2015 81:16–23. [PubMed: 26115911]
- [7]. Prez-Sez M, Prieto-Alhambra D, Barrios C, Crespo M, Redondo D, Nogus X, et al. Increased hip fracture and mortality in chronic kidney disease individuals: the importance of competing risks. *Bone*. 2015 73:154–9. [PubMed: 25549867]
- [8]. Basu U, Goodbrand J, Turdo ME, Donnan PT, McGilchrist M, Frost H, et al. Association between allopurinol use and hip fracture in older patients. *Bone*. 2016 84:189–193. [PubMed: 26769005]

- [9]. Cauley J, Cawthon P, Peters K, Cummings S, Ensrud K, Bauer D, et al. Risk Factors for Hip Fracture in Older Men: The Osteoporotic Fractures in Men Study (MrOS). *J Bone Miner Res* 2016 31(10):1810–1819. [PubMed: 26988112]
- [10]. Cox D, Oakes D. *Analysis of Survival Data*. Chapman and Hall; 1984.
- [11]. Cox DR. Regression Models and Life-Tables. *Journal of the Royal Statistical Society Series B (Methodological)*. 1972 34(2):187–220.
- [12]. Wolbers M, Koller M, Stel VS, Jager K, Le ondre K, Heinze G. Competing Risks Analyses: Objectives and Approaches. *European Heart Journal*. 2014 35:2936–2941. [PubMed: 24711436]
- [13]. Ferreira-Gonzalez I, Permyer-Miralda G, Busse JW, Bryant DM, Montori VM, Alonso-Coello P, et al. Methodologic discussions for using and interpreting composite endpoints are limited, but still identify major concerns. *Journal of Clinical Epidemiology*. 2007 60(7):651–657. [PubMed: 17573977]
- [14]. Fried LP, Borhani NO, Enright P, Furberg CD, Gardin JM, Kronmal RA, Kuller LH, Manolio TA, Mittelmark MB, Newman A, O'Leary DH, Psaty B, Rautaharju P, Tracy RP, Weiler PG. The Cardiovascular Health Study: design and rationale. *Ann Epidemiol* 1991 1 (3):263–276. [PubMed: 1669507]
- [15]. Wu Z-J, Zhao P, Liu B, Yuan Z-C (2016) Effect of Cigarette Smoking on Risk of Hip Fracture in Men: A Meta-Analysis of 14 Prospective Cohort Studies. *PLoS ONE* 11(12): e0168990 10.1371/journal.pone.0168990 [PubMed: 28036356]
- [16]. Shen GS, Li Y, Zhao G, Zhou HB, Xie ZG, Xu W, et al. Cigarette smoking and risk of hip fracture in women: a meta-analysis of prospective cohort studies. *Injury*. 2015; 46(7):1333–40. [PubMed: 25956674]
- [17]. Kanis JA, Johnell O, Oden A, Johansson H, De Laet C, Eisman JA, et al. Smoking and fracture risk: a meta-analysis. 2005. *Osteoporos Int* 16(2):155–62. [PubMed: 15175845]
- [18]. Daya NR, Voskertchian A, Schneider ALC, Ballew S, McAdams Demarco M, Coresh J, Appel LJ, Grams ME. Kidney Function and Fracture Risk: The Atherosclerosis Risk in Communities (ARIC) Study (2016). *American Journal of Kidney Diseases*, 67 (2), pp. 218–226. [PubMed: 26250781]
- [19]. Schneider ALC, Williams EK, Brancati FL, Blecker S, Coresh J, Selvin E. Diabetes and Risk of Fracture-Related Hospitalization: The Atherosclerosis Risk in Communities Study. *Diabetes Care*. 2013 36(5):1153–1158. doi:10.2337/dc12-1168 [PubMed: 23248194]
- [20]. R Development Core Team (2018) R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing: Vienna ISBN 3-900051-07-0. <http://www.R-project.org>.

Table 1:

Descriptive characteristics of the CHS population at the 1992/93 visit. We provide mean $\pm$ standard deviation for continuous variables and percentages for categorical variables.

	Total	Women	Men
	5265	3099	2166
Age (years)	75.13 $\pm$ 5.51	74.84 $\pm$ 5.39	75.55 $\pm$ 5.67
Black Race	16.8%	18%	15.1%
Good Health	77.4%	76.2%	79.2%
Education($\geq$ 12 gr)	44.8%	41.4%	49.7%
Diabetes	16.5%	14.6%	19.3%
ADL difficulty	11.8%	14%	8.6%
Fall	16.2%	19.6%	11.3%
Systolic BP (mmHg)	136.6 $\pm$ 21.66	137.46 $\pm$ 21.92	135.38 $\pm$ 21.24
Diastolic BP (mmHg)	71.28 $\pm$ 11.59	70.38 $\pm$ 11.57	72.56 $\pm$ 11.49
Glucose (mg/dL)	108.47 $\pm$ 35.61	106.9 $\pm$ 35.6	110.64 $\pm$ 35.52
Insulin (mIU/L)	14.29 $\pm$ 24.12	14.05 $\pm$ 23.56	14.61 $\pm$ 24.88
Current smoking	9.8%	10.1%	9.5%
Cystatin C eGFR (mL/min/1.73 m ²)	72.53 $\pm$ 19.03	74.83 $\pm$ 19.19	69.31 $\pm$ 18.32

Table 2:

Hazard ratio estimates for incident hip fracture, mortality, and the composite event. For hip fracture, the cause-specific (CS) Cox approach is contrasted with the Fine-Gray (FG) approach. A model adjusting for age, race, and gender.

5 years of increased age	HR	95%CI	p-value
Hip fracture, CS	1.74	(1.61,1.87)	<0.01
Hip fracture, FG	1.16	(1.09,1.24)	<0.01
Composite event	1.70	(1.66,1.75)	<0.01
Mortality	1.72	(1.67,1.77)	<0.01
Male			
Hip fracture, CS	0.62	(0.53,0.74)	<0.01
Hip fracture, FG	0.49	(0.41,0.58)	<0.01
Composite event	1.31	(1.23,1.38)	<0.01
Mortality	1.41	(1.33,1.49)	<0.01
Black			
Hip fracture, CS	0.39	(0.29,0.52)	<0.01
Hip fracture, FG	0.38	(0.29,0.51)	<0.01
Composite event	0.99	(0.92,1.07)	0.82
Mortality	1.05	(0.97,1.14)	0.21

Table 3:

Hazard ratio estimates for incident hip fracture, mortality, and the composite event. For hip fracture, the cause-specific (CS) Cox approach is contrasted with the Fine-Gray (FG) approach. Separate models for each risk factor, each model also adjusting for age, race, and gender.

	HR	95%CI	p-value
Current smoking			
Hip fracture, CS	1.66	(1.28,2.14)	<0.01
Hip fracture, FG	1.17	(0.9,1.51)	0.24
Composite event	1.59	(1.44,1.76)	<0.01
Mortality	1.58	(1.44,1.75)	<0.01
Diabetes			
Hip fracture, CS	1.19	(0.94,1.52)	0.15
Hip fracture, FG	0.79	(0.62,1.01)	0.06
Composite event	1.66	(1.53,1.8)	<0.01
Mortality	1.69	(1.56,1.84)	<0.01
Cystatin C-based eGFR (per 15 ml/minute/1.73m ²)			
Hip fracture, CS	0.95	(0.89,1.02)	0.19
Hip fracture, FG	1.09	(1.02,1.17)	<0.01
Composite event	0.81	(0.79,0.83)	<0.01
Mortality	0.79	(0.77,0.81)	<0.01