Comorbidity and Survival for Older Men with Prostate Cancer

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Presentation summary

- Why consider comorbid disease?
- Measuring comorbid disease
- Estimating the effects of comorbid disease
- Conclusions

Why consider comorbid disease?

- Comorbidities are conditions that influence patient survival, other than prostate cancer.
- Measurement of comorbid disease and its effects can inform prognosis, treatment decision making, and comparisons of outcomes across institutions.

How should comorbid disease be measured?

- Charlson index (NCI)
- Elixhauser (AHRQ)
- Global ICD-9-CM

Data sources for measuring comorbidity

- Clinical trials
- Prospective cohorts
- Retrospective cohorts

SEER-Medicare

- SEER Cancer registry data
- Tumor stage and grade reported
- Medicare hospital and physicians claims for events before and after diagnosis

Study population

- 54,799 men diagnosed in 1995 – 1998
- Medicare eligible 1 year prior to diagnosis
- Comorbid disease measured by retrospective review of ICD-9-CM reported in Medicare claims prior to diagnosis
- Social Security Administration reported survival known through 2003 (complete 5 year follow-up)

Study population

Death within five years of diagnosis	40.3
Mean age at diagnosis	75.0
Radical prostatectomy within six months of diagnosis	13.7
Clinical Stage	
T1: Clinically inapparent tumor	32.0
T2: Localized disease	48.1
T3: Extension of tumor beyond prostate	3.2
T4: Tumor invading bladder neck, other areas adjacent to prostate	1.1
M1: Distant metastasis	6.2
Unk: Tumor characterization unknown	9.4

Study population

Grade	
1: Gleason 2-4, well differentiated	10.6
2: Gleason 5-7, moderately differentiated	58.1
3: Gleason 8-10, poorly differentiated	20.9
4: Undifferentiated, anaplastic	0.5
Unknown differentiated, not stated, or not applicable	9.8

Study population

Frequently occurring ICD-9-CM diagnosis codes

4011: Essential hypertension, benign	14.18
2724: Disorders of lipoid metabolism, unspecified hyperlipidemia	10.20
25000: Diabetes mellitus without mention of complication, type II	10.17
7020: Dermatoses, actinic keratosis	9.33
2720: Disorders of lipoid metabolism, pure hypercholesterolemia	9.28
496: Chronic airway obstruction	8.92
36616: Senile cataract, nuclear sclerosis	8.53
78609: Dyspnea and other respiratory abnormalities	7.64
5997: Hematuria	7.00
4140: Coronary atherosclerosis, of unspecified type of vessel	6.30

Multivariable logistic regression

- Probability of survival at five years, adjusted for model covariates

$$\text{logit}\,\text{prob}(\text{Y}=1|\,\mathbf{X}) = \alpha + \beta\mathbf{X}$$

Multivariable logistic regression

- Base model: Stage, Grade, Age, RP
- Base model + Charlson index
- Base model + Elixhauser (30 comorbidities)
- Base model + Global ICD (156 comorbidities)

Comparison of validated statistical performance

- C index
- 0.76 Base model
- 0.77 Base model + Charlson index
- 0.78 Base model + Elixhauser
- 0.80 Base model + Global ICD-9-CM

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Comparison of validated statistical performance

- Nagelkerke index
- 0.28 Base model
- 0.31 Base model + Charlson index
- 0.32 Base model + Elixhauser
- 0.36 Base model + Global ICD-9-CM

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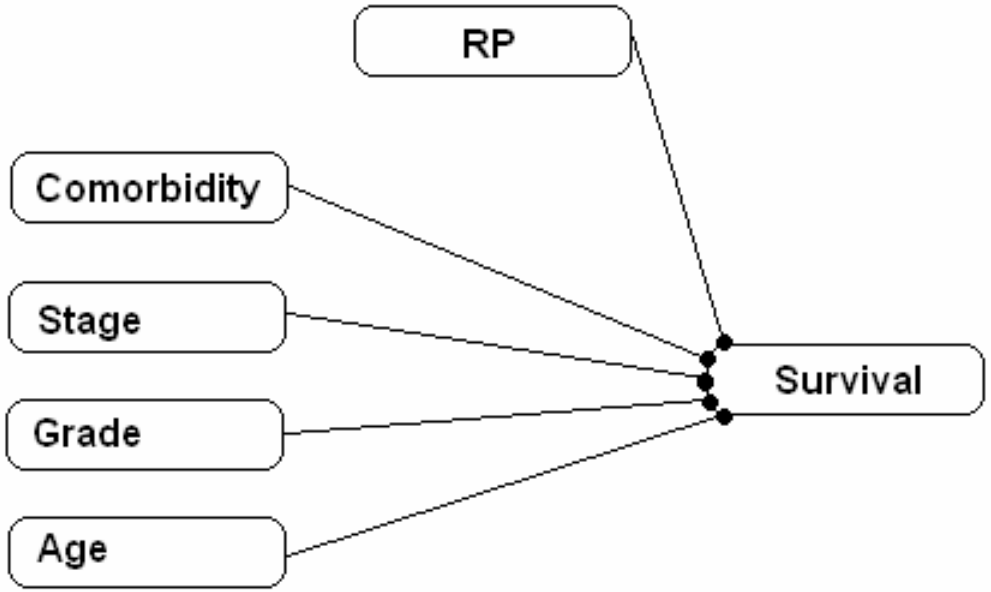
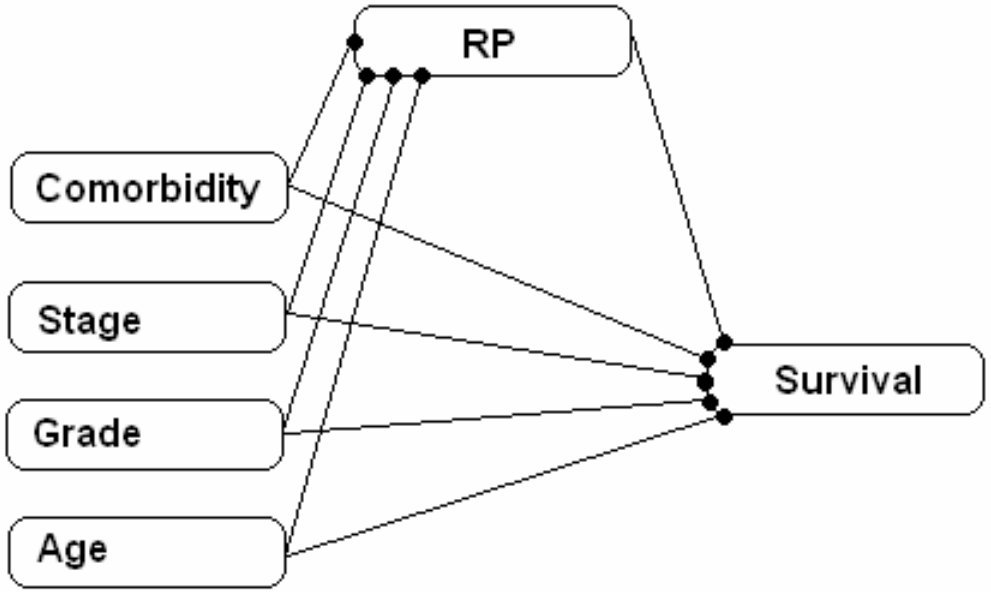
Estimating the effects of comorbid disease

- Logistic regression allows only direct effects



Estimating the effects of comorbid disease

- Reality is more complex



Subpopulation with localized prostate cancer

- Define subpopulation including only potential candidates for radical prostatectomy
- Subset of study population with stages T1, T2, with well or moderately differentiated tumors
- 33,394 patients included in subpopulation
- Quantify predictive information obtained from comorbid disease

Define matched population with propensity score

- Estimate probability of treatment assignment in original study population
- Use estimates to create matched population
- Include only patients in matched population with localized disease
- Assess balance achieved in matched population
- Quantify predictive information obtained from comorbid disease

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Propensity matched study population

	RP	Match	P value
Total cases	5682	5771	
Mean age at diagnosis	70.1	70.1	0.8618
Clinical Stage			
T1: Clinically inapparent tumor	42.4	43.4	0.2671
T2: Localized disease	57.6	56.6	0.2671
Grade			
1: Gleason 2-4, well differentiated	7.6	8.0	0.2460
2: Gleason 5-7, moderately differentiated	92.6	92.0	0.2460

Propensity score matched

	RP	Match	P value
Comorbid disease			
4011: Essential hypertension, benign	16.2	16.3	0.9281
2724: Unspecified hyperlipidemia	13.7	14.3	0.3856
25000: Diabetes mellitus, no complications, type II	8.5	8.5	0.9351
7020: Dermatoses, actinic keratosis	13.6	13.1	0.4602
2720: Pure hypercholesterolemia	14.0	14.9	0.2101
496: Chronic airway obstruction	5.5	5.6	0.8052
36616: Senile cataract, nuclear sclerosis	8.3	7.9	0.4747
78609: Dyspnea, other respiratory abnormalities	5.6	5.5	0.8721
5997: Hematuria	5.7	6.6	0.0413
4140: Coronary atherosclerosis, unspecified	5.0	5.8	0.0740

Compare predictive information

- Predictive information from comorbidity in subpopulation with localized prostate cancer is confounded by treatment assignment
- Predictive information from comorbidity in the matched population is not confounded, because the matching adjusts for treatment assignment
- Comparing the predictive information in the two groups provides evidence about the amount of confounding present in the subpopulation

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Quantifying predictive information

- Proportion of log likelihood explained only by comorbid disease covariates compared to that explained by entire set of model covariates
- Akaike's Information Criterion provides penalty for model complexity
- Method used by Calif et al. to quantify predictive information contributed by coronary disease covariates used to predict survival

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Quantifying predictive information

$$\text{Proportion of log likelihood explained by subset} = \frac{\text{LR}_{\text{Subset}}\ \chi^2}{\text{LR}_{\text{Global}}\ \chi^2}$$

$$\text{LR}_{\text{Subset}}\ \chi^2 = [(\text{-2 log L intercept only}) - (\text{-2 log L covariate subset})]$$

$$\text{LR}_{\text{Global}}\ \chi^2 = [(\text{-2 log L intercept only}) - (\text{-2 log L all covariates})]$$

Results

Proportion of log likelihood explained by comorbidity	
Localized disease patients in original population	58%
Localized disease patients in matched population	64%

Conclusions

- Global ICD-9-CM model has meaningfully better statistical performance than other models
- Logistic regression model underestimates total effect of comorbid disease on survival at 5 years

Limitations

- Why not Cox Proportional Hazards regression?
- Analysis does not include radiation therapy or other treatment
- Effects of comorbid disease on other covariates not addressed

Whats next?

- Marginal structural models
- Structural equation models

Contributors

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