Diagnostic Accuracy and Prediction Increment of Markers of Epithelial-Mesenchymal Transition to Assess Cancer Cell Detachment from Primary Tumors

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Additional File 2: Supplemental Results

Table S1. Reclassification of 5-year risk of all-cause mortality among colorectal cancer patients by continuous E-cadherin (n=188)

5-year risk from model without E-cadherin	5-year risk from model with continuous E-cadherin				
	0-20%	20-30%	30-40%	>40%	Total
0-20%					
Participants, n	0	0	0	0	0
Deaths, n	0	0	0	0	0
5-year risk, %	0	0	0	0	0
20-30%					
Participants, n	40	43	15	1	99
Deaths, n	7	10	6	0	23
5-year risk, %	17.3	23.0	38.7	0	22.4
30-40%					
Participants, n	2	12	21	31	66
Deaths, n	1	4	4	15	24
5-year risk, %	39.3	32.0	18.6	47.6	37.5
>40%					
Participants, n	0	1	0	22	23
Deaths, n	0	0	0	15	15
5-year risk, %	0	0	0	66.6	66.0
Total					
Participants, n	42	56	36	54	188
Deaths, n	8	14	10	30	62
5-year risk, %	15.4	25.0	34.4	54.8	33.0

Model without E-cadherin includes standard diagnostic tests of lymph node evaluation and radiologic imaging (each coded as dichotomous positive versus negative). For both predictors, a positive result means evidence supporting detachment of cancer cells from the primary tumor and

a negative result means no evidence of detachment. Model with E-cadherin includes standard diagnostic tests and cellular membrane E-cadherin expression measured by immunohistochemistry in primary tumor cancer cells on a continuous average intensity scale (0-3). Both models are Cox proportional hazards models of time from cancer diagnosis to all-cause mortality, censored at 5 years after diagnosis. Cut points to define mortality risk categories were 20%, 30%, and 40%. Numbers of participants and deaths are observed counts. Reported risks are predicted risks.

Table S2. Reclassification of 5-year risk of all-cause mortality among colorectal cancer patients by E-cadherin dichotomized at 0.52 (n=188)

5-year risk from model without E-cadherin	5-year risk from model with E-cadherin dichotomized at 0.52				
	0-20%	20-30%	30-40%	>40%	Total
0-20%					
Participants, n	0	0	0	0	0
Deaths, n	0	0	0	0	0
5-year risk, %	0	0	0	0	0
20-30%					
Participants, n	93	0	0	6	99
Deaths, n	20	0	0	3	23
5-year risk, %	21.4	0	0	46.0	22.4
30-40%					
Participants, n	0	0	61	5	66
Deaths, n	0	0	20	4	24
5-year risk, %	0	0	32.5	72.3	37.5
>40%					
Participants, n	0	0	0	23	23
Deaths, n	0	0	0	15	15
5-year risk, %	0	0	0	63.8	66.0
Total					
Participants, n	93	0	61	34	188
Deaths, n	20	0	20	22	62
5-year risk, %	20.0	0	34.6	66.4	33.0

Model without E-cadherin includes standard diagnostic tests of lymph node evaluation and radiologic imaging (each coded as dichotomous positive versus negative). Model with E-cadherin includes standard diagnostic tests and cellular membrane E-cadherin expression measured by immunohistochemistry in primary tumor cancer cells on a continuous average intensity scale (0-3), then dichotomized at 0.52 (coded as dichotomous positive versus negative). For all predictors, a positive result means evidence supporting detachment of cancer cells from the primary tumor and a negative result means no evidence of detachment. Both models are Cox proportional hazards models of time from cancer diagnosis to all-cause mortality, censored at 5 years after diagnosis. Cut points to define mortality risk categories were 20%, 30%, and 40%. Numbers of participants and deaths are observed counts. Reported risks are predicted risks.

Table S3. Reclassification of 5-year risk of all-cause mortality among colorectal cancer patients by E-cadherin dichotomized at 0.60 (n=188)

5-year risk from model without E-cadherin	5-year risk from model with E-cadherin dichotomized at 0.60				
	0-20%	20-30%	30-40%	>40%	Total
0-20%					
Participants, n	0	0	0	0	0
Deaths, n	0	0	0	0	0
5-year risk, %	0	0	0	0	0
20-30%					
Participants, n	83	0	0	16	99
Deaths, n	17	0	0	6	23
5-year risk, %	20.3	0	0	36.3	22.4
30-40%					
Participants, n	0	0	55	11	66
Deaths, n	0	0	17	7	24
5-year risk, %	0	0	30.6	60.8	37.5
>40%					
Participants, n	0	0	0	23	23
Deaths, n	0	0	0	15	15
5-year risk, %	0	0	0	63.8	66.0
Total					
Participants, n	83	0	55	50	188
Deaths, n	17	0	17	28	62
5-year risk, %	19.0	0	33.0	56.7	33.0

Model without E-cadherin includes standard diagnostic tests of lymph node evaluation and radiologic imaging (each coded as dichotomous positive versus negative). Model with E-cadherin includes standard diagnostic tests and cellular membrane E-cadherin expression measured by immunohistochemistry in primary tumor cancer cells on a continuous average intensity scale (0-3), then dichotomized at 0.60 (coded as dichotomous positive versus negative). For all predictors, a positive result means evidence supporting detachment of cancer cells from the primary tumor and a negative result means no evidence of detachment. Both models are Cox proportional hazards models of time from cancer diagnosis to all-cause mortality, censored at 5 years after diagnosis. Cut points to define mortality risk categories were 20%, 30%, and 40%. Numbers of participants and deaths are observed counts. Reported risks are predicted risks.

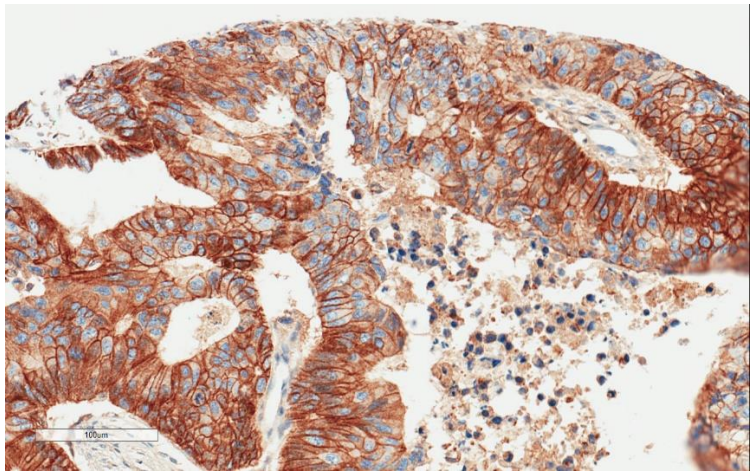
Table S4. Reclassification of 5-year risk of all-cause mortality among colorectal cancer patients by E-cadherin dichotomized at 0.85 (n=188)

5-year risk from model without E-cadherin	5-year risk from model with E-cadherin dichotomized at 0.85				
	0-20%	20-30%	30-40%	>40%	Total
0-20%					
Participants, n	0	0	0	0	0
Deaths, n	0	0	0	0	0
5-year risk, %	0	0	0	0	0
20-30%					
Participants, n	43	56	0	0	99
Deaths, n	8	15	0	0	23
5-year risk, %	18.3	26.5	0	0	22.4
30-40%					
Participants, n	0	25	0	41	66
Deaths, n	0	7	0	17	24
5-year risk, %	0	27.4	0	41.0	37.5
>40%					
Participants, n	0	0	2	21	23
Deaths, n	0	0	0	15	15
5-year risk, %	0	0	0	69.7	66.0
Total					
Participants, n	43	81	2	62	188
Deaths, n	8	22	0	32	62
5-year risk, %	15.0	27.3	38.0	53.3	33.0

Model without E-cadherin includes standard diagnostic tests of lymph node evaluation and radiologic imaging (each coded as dichotomous positive versus negative). Model with E-cadherin includes standard diagnostic tests and cellular membrane E-cadherin expression measured by immunohistochemistry in primary tumor cancer cells on a continuous average intensity scale (0-3), then dichotomized at 0.85 (coded as dichotomous positive versus negative). For all predictors, a positive result means evidence supporting detachment of cancer cells from the primary tumor and a negative result means no evidence of detachment. Both models are Cox proportional hazards models of time from cancer diagnosis to all-cause mortality, censored at 5 years after diagnosis. Cut points to define mortality risk categories were 20%, 30%, and 40%. Numbers of participants and deaths are observed counts. Reported risks are predicted risks.

Figure S1. E-cadherin immunohistochemistry staining of positive and negative cores

A. Positive staining



B. Negative staining

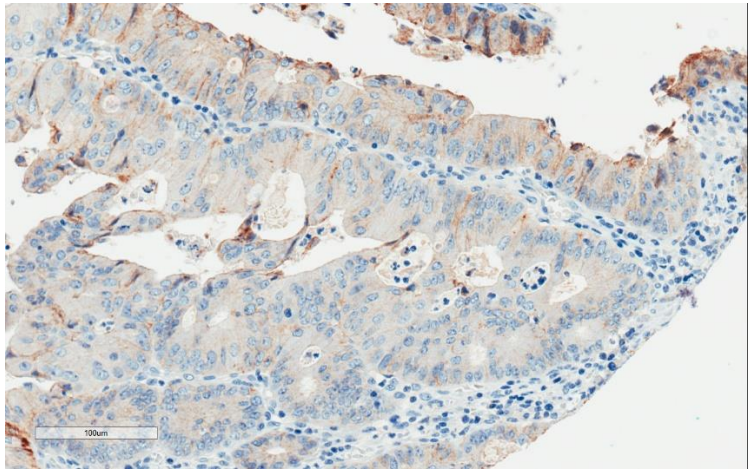
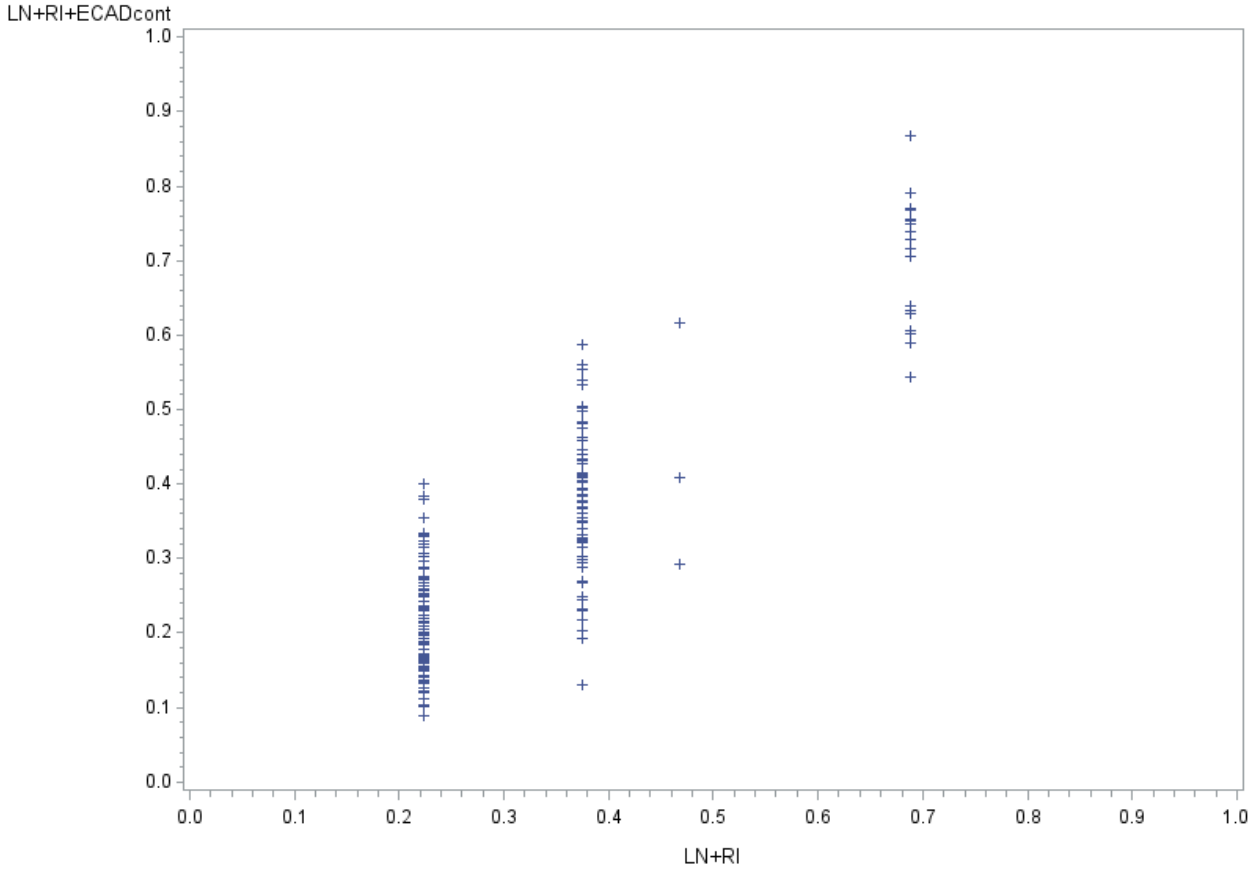


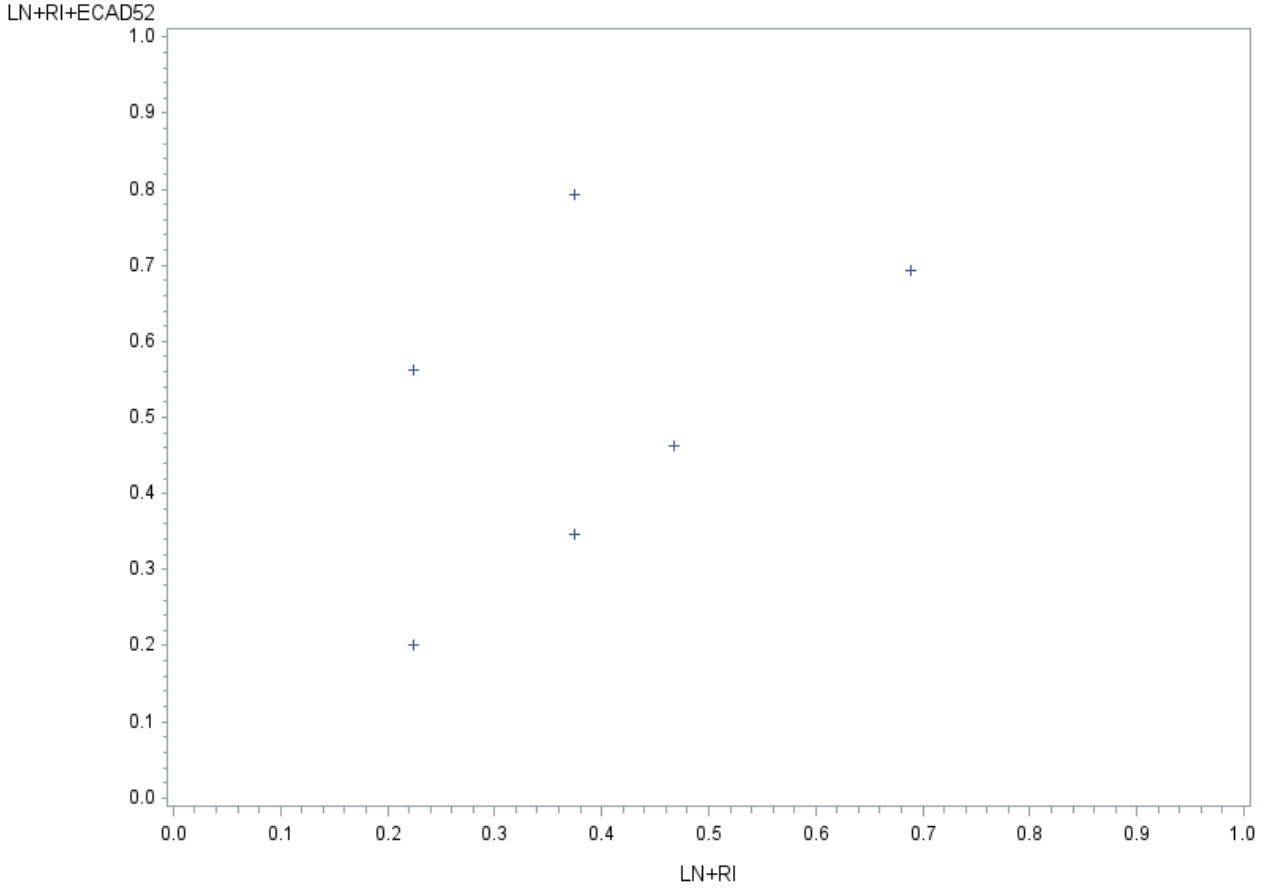
Figure S2. Predicted probabilities of colorectal cancer case all-cause mortality within 5 years of diagnosis for predictors of lymph node evaluation and radiologic imaging, either with or without further predictor of continuous E-cadherin (n=188)



All models were Cox proportional hazards models of time from colorectal cancer diagnosis to all-cause mortality, censored at 5 years. Models included predictors of lymph node evaluation (present vs. absent cancer cells) and radiologic imaging (present vs. absent cancer cells), and either did or did not further include measurement of E-cadherin in primary tumor cancer cells (continuous average intensity scale of 0-3).

LN=lymph node evaluation, ECADcont=continuous E-cadherin, RI=radiologic imaging

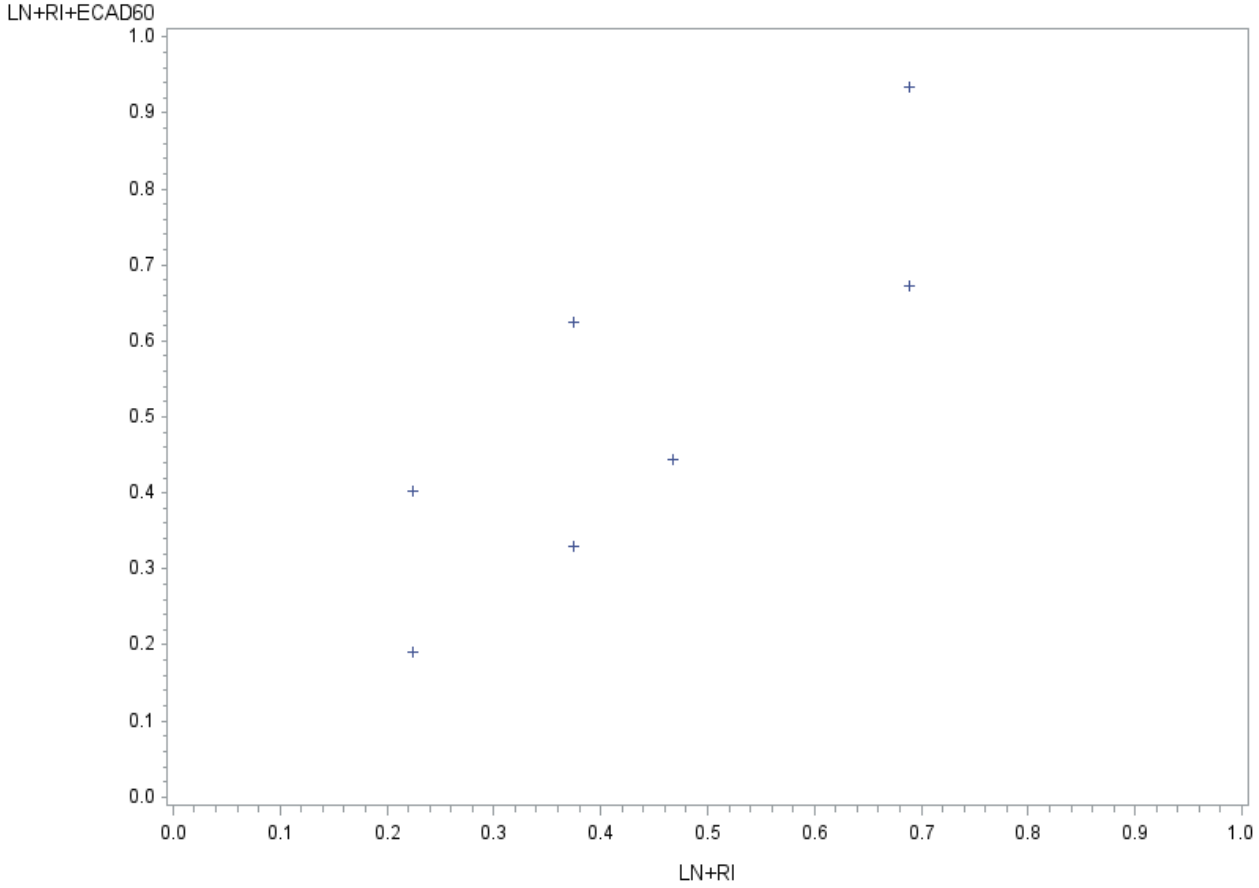
Figure S3. Predicted probabilities of colorectal cancer case all-cause mortality within 5 years of diagnosis for predictors of lymph node evaluation and radiologic imaging, either with or without further predictor of E-cadherin dichotomized at 0.52 (n=188)



All models were Cox proportional hazards models of time from colorectal cancer diagnosis to all-cause mortality, censored at 5 years. Models included predictors of lymph node evaluation (present vs. absent cancer cells) and radiologic imaging (present vs. absent cancer cells), and either did or did not further include measurement of E-cadherin in primary tumor cancer cells (continuous average intensity scale of 0-3, then dichotomized at 0.52).

LN=lymph node evaluation, ECAD52=E-cadherin dichotomized at 0.52, RI=radiologic imaging

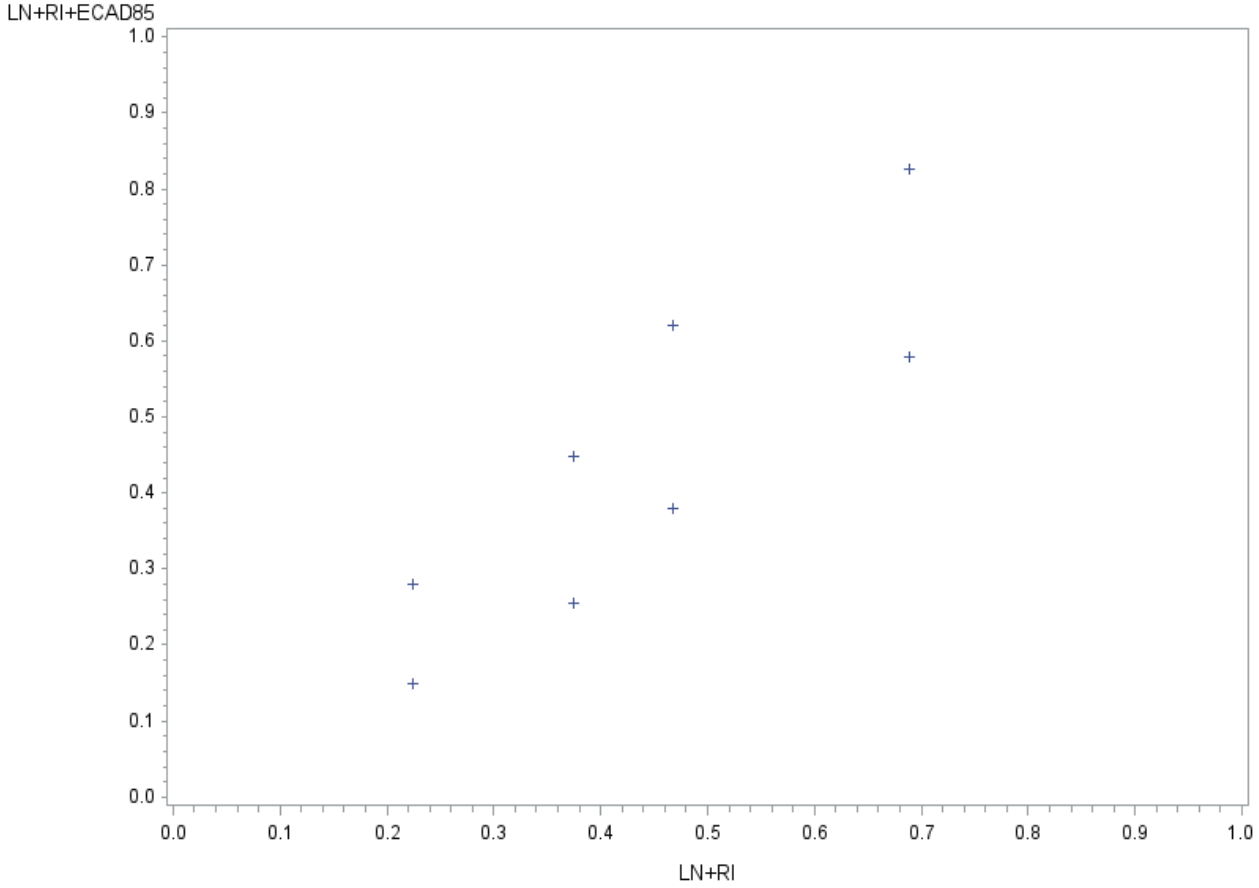
Figure S4. Predicted probabilities of colorectal cancer case all-cause mortality within 5 years of diagnosis for predictors of lymph node evaluation and radiologic imaging, either with or without further predictor of E-cadherin dichotomized at 0.60 (n=188)



All models were Cox proportional hazards models of time from colorectal cancer diagnosis to all-cause mortality, censored at 5 years. Models included predictors of lymph node evaluation (present vs. absent cancer cells) and radiologic imaging (present vs. absent cancer cells), and either did or did not further include measurement of E-cadherin in primary tumor cancer cells (continuous average intensity scale of 0-3, then dichotomized at 0.60).

LN=lymph node evaluation, ECAD60=E-cadherin dichotomized at 0.60, RI=radiologic imaging

Figure S5. Predicted probabilities of colorectal cancer case all-cause mortality within 5 years of diagnosis for predictors of lymph node evaluation and radiologic imaging, either with or without further predictor of E-cadherin dichotomized at 0.85 (n=188)



All models were Cox proportional hazards models of time from colorectal cancer diagnosis to all-cause mortality, censored at 5 years. Models included predictors of lymph node evaluation (present vs. absent cancer cells) and radiologic imaging (present vs. absent cancer cells), and either did or did not further include measurement of E-cadherin in primary tumor cancer cells (continuous average intensity scale of 0-3, then dichotomized at 0.85).

LN=lymph node evaluation, ECAD85=E-cadherin dichotomized at 0.85, RI=radiologic imaging