Scientific Article

Improving prediction of surgical resectability over current staging guidelines in patients with pancreatic cancer who receive stereotactic body radiation therapy

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Abstract

Purpose: For patients with localized pancreatic cancer (PC) with vascular involvement, prediction of resectability is critical to define optimal treatment. However, the current definitions of borderline resectable (BR) and locally advanced (LA) disease leave considerable heterogeneity in outcomes within these classifications. Moreover, factors beyond vascular involvement likely affect the ability to undergo resection. Herein, we share our experience developing a model that incorporates

detailed radiologic, patient, and treatment factors to predict surgical resectability in patients with BR and LA PC who undergo stereotactic body radiation therapy (SBRT).

Methods and materials: Patients with BR or LA PC who were treated with SBRT between 2010 and 2016 were included. The primary endpoint was margin negative resection, and predictors included age, sex, race, treatment year, performance status, initial staging, tumor volume and location, baseline and pre-SBRT carbohydrate antigen 19-9 levels, chemotherapy regimen and duration, and radiation dose. In addition, we characterized the relationship between tumors and key arteries (superior mesenteric, celiac, and common hepatic arteries), using overlap volume histograms derived from computed tomography data. A classification and regression tree was built, and leave-one-out cross-validation was performed. Prediction of surgical resection was compared between our model and staging in accordance with the National Comprehensive Care Network guidelines using McNemar's test.

Results: A total of 191 patients were identified (128 patients with LA and 63 with BR), of which 87 patients (46%) underwent margin negative resection. The median total dose was 33 Gy. Predictors included the chemotherapy regimen, amount of arterial involvement, and age. Importantly, radiation dose that covers 95% of gross tumor volume (GTV D95), was a key predictor of resectability in certain subpopulations, and the model showed improved accuracy in the prediction of margin negative resection compared with National Comprehensive Care Network guideline staging (75% vs 63%; $P < .05$).

Conclusions: We demonstrate the ability to improve prediction of surgical resectabiliy beyond the current staging guidelines, which highlights the value of assessing vascular involvement in a continuous manner. In addition, we show an association between radiation dose and resectability, which suggests the potential importance of radiation to allow for resection in certain populations. External data are needed for validation and to increase the robustness of the model.

Introduction

The prognosis for patients with pancreatic cancer (PC) remains poor with a 5-year overall survival rate of <5%.[1] Unfortunately, lack of effective screening tests and the late development of symptoms result in roughly 50% to 60% of patients having metastatic disease at the time of presentation.[2] For patients with nonmetastatic disease, the initial assessment of resectability is critical because complete surgical resection is a requirement for long-term disease-free survival.

Triple-phase, contrast-enhanced, thin-slice, multi-detector, row helical computed tomography (CT) with 3-dimensional reconstruction serves as the preferred modality to visualize the relationship between tumor and nearby critical vasculature and thereby determines the resectability.[3–8] Multiple criteria have been developed to classify the likelihood of resectability on the basis of imaging findings, which have supplemented traditional American Joint Committee on Cancer staging to characterize prognosis and help dictate treatment algorithms as reflected by the most recent National Comprehensive Care Network (NCCN) guidelines.[3,9–12]

Nevertheless, considerable heterogeneity in outcomes exists within the current definitions of resectable, borderline resectable (BR), and locally advanced (LA) disease. As an example, recent national trials have reported low rates of surgical resection for patients with LA disease, but single-institution series from high-volume centers have indicated much higher rates of resection.[13–15] A similar variation exists among patients with BR disease.[16,17] Some of this variation stems from differences in institutional practice patterns, but heterogeneity in vascular involvement that is not captured in the current definitions for BR and LA disease and variations in patient and treatment characteristics also drive these variations. As such, more robust models that better characterize the likelihood of resection would be helpful.

Herein, we share our experience with developing such a model that uses a more sophisticated radiologic analysis of tumor relationship with critical vasculature and also incorporates patient and treatment variables to better predict the likelihood of resection in patients with BR and LA disease. Of note, because the practice pattern at our institution is to administer neoadjuvant chemotherapy followed by stereotactic body radiation therapy (SBRT) for patients with BR or LA disease, this model is specific to patients undergoing this treatment paradigm. In addition, given the relative infancy of this treatment approach for patients with PC, this model is also in its infancy. Nevertheless, we share our early experience with this model to show the potential to build upon the current imperfect tools to predict resectability. Our hope is to inspire similar efforts at other institutions and develop collaborative efforts that improve the way in which we care for this patient population.

Methods and materials

Patient selection

We included patients with BR or LA PC per the NCCN guidelines and who were treated with SBRT between 2010 and 2016. All patients were treated with a total dose of 25 Gy to 33 Gy in 5 fractions. Prescription doses below 33 Gy were due to proximity of gastrointestinal luminal structures. Only patients with complete radiation treatment dosimetry data were included. Patients with metastatic disease or treatment with palliative intent were excluded.

Contouring and dosimetry collection

Our institutional workflow for pancreatic SBRT has been previously described.[18,19] With respect to target contouring on planning CT, the gross tumor volume (GTV) included the primary tumor and a separate clinical tumor volume was not used. The delineation of the planning tumor volume (PTV) depended on the type of motion management strategy that was employed. For patients treated with active breathing control (ABC), the PTV was created by initially expanding the GTV by a 2-mm margin and then excluding portions of the volume that were within 2 mm of the bowel, stomach, or duodenum (Suppl Fig 1). Patients who were unable to comply with the ABC technique were treated under free-breathing conditions. In this scenario, an internal target volume was created from the union of GTVs on the maximal excursion phases as identified on a 4-dimensional planning CT scan. The PTV was subsequently created by expanding the internal target volume in a manner similar to the ABC scenario.

The celiac axis (CA), superior mesenteric artery (SMA), and common hepatic artery (CHA) were retrospectively contoured on planning CTs by 2 trained investigators who were blinded to the study outcome. Specifically, the CA was contoured from its takeoff from the aorta to its bifurcation into the CHA and splenic arteries. The SMA was contoured from its takeoff from the aorta for a distance of three centimeters. The CHA was contoured from the celiac bifurcation for a distance of 1 cm.

Data preprocessing and overlap volume-histogram analysis

All contours were transferred to the Oncospace database,[20–23] and both dose-volume and overlap-volume histograms (OVHs) were created.[24–27] The OVH is a distance transform that quantifies the spatial relationship between 2 objects, which in this case is between the GTV and key arterial structures (CA, SMA, and CHA). The minimum distances between the GTV and arterial structures derived from the OVH were used to assess the respective shape relationships.[24–27] Specifically, the distance between GTV and arterial vessels was calculated by the degree of expansion or contraction of GTV that was required to result in abutment of the arterial structures. In this framework, a nonzero volume at a negative OVH distance indicated overlap of some portion of the volumes. The distances between the GTV and CA, SMA, and CHA were referred to as d_{CA}, d_{SMA}, and d_{CHA}, respectively.

Tumors often involve more than 1 arterial structure; therefore, nomenclature was devised to describe the distance to the arterial structure that was the closest to the tumor or most involved with the tumor. Specifically, $d_{CA,SMA,CHA}^{min}$, was defined as the minimum value among the distances from the GTV to the CA, SMA, and CHA, and $d_{CA,SMA}^{min}$ as the minimum value among the distances from the GTV to the CA and SMA. For example, if a tumor was 1 cm away from the SMA, 0.5 cm into CA, and 0.7 cm into CHA, then $d_{SMA} = 1.0$, $d_{CA} = -0.5$, $d_{CHA} = -0.7$, $d_{CA,SMA,CHA}^{min} = -0.7$, and $d_{CA,SMA}^{min} = -0.5$.

Statistical analysis

We explored the associations between treatment and tumor characteristics and the primary outcome of margin negative resection. Variables that were examined included age, sex, race, performance status, treatment year, initial staging (BR or LA), tumor location as designated by the diagnostic radiologist (head, body, or tail), GTV volume, GTV D95, d_{CA}, d_{SMA}, d_{CHA}, $d_{CA,SMA}^{min}$, $d_{CA,SMA,CHA}^{min}$, chemotherapy regimen (FOLFIRINOX, gemcitabine/nab-paclitaxel, other multi-agent, gemcitabine alone, or none), chemotherapy duration (≥ 4 or <4 months), and baseline and pre-SBRT carbohydrate antigen 19-9 (CA19-9) values. The association of continuous variables with resection was tested either by Student t test or Wilcoxon rank-sum test, and the χ^2 test was used for categorical variables.

A decision tree was built to predict the likelihood of eventual surgical resection, using the Classification and Regression Trees (CART) algorithm.[28] The total cohort was partitioned into 2 subgroups on the basis of the predictor variable that portended the highest statistical risk of being resected. This process was repeated for each derived subset in an iterative manner. At each partition, an information gain criterion was applied to determine partitioning predictor variables with binary thresholds for continuous or ordinal variables and binary partitioning categories for nominal variables. The size of the tree (ie, number of predictor variables selected in the decision tree model) was determined by growing and subsequently pruning the tree to achieve the highest area under the curve in the leave-one-out cross validation. Next, the

model performance was calculated. Lastly, McNemar's test was used to assess whether the CART model improved the prediction of surgical resection compared with the NCCN disease stage.[7]

All statistical analyses were performed with R software v3.1.2 (R Foundation Project, Auckland, New Zealand). A *P*-value of < .05 was considered statistically significant.

Results

A total of 191 patients fit the inclusion criteria. The patient and treatment characteristics are summarized in Table 1. The mean age for the cohort was 64 years, approximately half of the patients (51%) were male, and the majority (85%) were Caucasian. Most patients were treated with multi-agent chemotherapy (n = 148; 77%), but a minority of patients received single-agent gemcitabine (n = 36; 19%) or no chemotherapy (n = 7; 4%). Almost half of the patients (n = 94; 49%) received >4 months of systemic therapy. Nearly 65% of patients had a CA19-9 level of ≥90 U/ml at baseline, but only 33% of patients had a CA19-9 level of ≥90 U/ml before SBRT. The median prescribed SBRT dose was 33 Gy (range, 25-33 Gy). The majority of patients (67%) was classified as LA per the NCCN guidelines, and the remaining 33% were classified as BR. The majority of the tumors were located at the pancreas head (64%).

Distribution of treatment year is also demonstrated in Table 1. After SBRT, 113 patients (59%) were explored, and 87 of these patients (46%) achieved a margin negative resection. Of the patients who were explored without a margin negative resection, 16 patients (8%) had positive margins, 7 patients (4%) underwent irreversible electroporation only, and 3 patients (2%) aborted treatment because of advanced disease.

Table 2 shows the tumor and treatment characteristics, stratified by NCCN definitions of BR and LA disease. The GTV D95 did not differ between patients with BR and LA disease but as expected, the LA group had larger GTVs and significantly more involvement of the major arteries. For example, in patients with BR disease, the GTV was an average of 1.21 cm away from the CA, but the GTV in patients with LA disease was an average of 0.32 cm away from the CA (*P* < .01). The GTV was also significantly further away on average from the SMA in patients with BR disease compared with patients with LA disease (0.22 vs −0.32 cm; *P* < .01). Similar findings were observed with respect to the CHA (0.84 vs 0.22 cm; *P* < .01). These trends were also reflected in similar differences between patients with BR and LA disease in mean $d^{min}_{CA,SMA,CHA}$ and $d^{min}_{CA,SMA}$. Notably, mean $d^{min}_{CA,SMA,CHA}$ and $d^{min}_{CA,SMA}$ were negative for the LA cohort, which indicates that patients

with LA disease had at least 1 arterial structure that was involved with tumor, but this was not true for the BR cohort.

Table 1 Study population characteristics (n = 191)

Parameters	
Age, *mean (SD)*	64.64 (9.87)
Prescription dose (Gy), *median*	33
Sex	
Male, *n (%)*	98 (51.30)
Female, *n (%)*	93 (48.70)
Race	
Caucasian, *n (%)*	162 (84.81)
Others, *n (%)*	29 (15.18)
Staging	
Borderline resectable, *n (%)*	63 (32.98)
Locally advanced, *n (%)*	128 (67.02)
Tumor location	
Head, *n (%)*	122 (63.87)
Body, *n (%)*	60 (31.41)
Tail, *n (%)*	6 (3.14)
Other, *n (%)*	3 (1.57)
Treatment year	
2010, *n (%)*	5 (2.62)
2011, *n (%)*	11 (5.76)
2012, *n (%)*	19 (9.95)
2013, *n (%)*	28 (14.66)
2014, *n (%)*	47 (24.60)
2015, *n (%)*	65 (34.03)
2016, *n (%)*	16 (8.38)
Chemotherapy	
Gemcitabine alone, *n (%)*	36 (18.85)
FOLFIRINOX, *n (%)*	78 (40.84)
Gemcitabine/nab-paclitaxel, *n (%)*	32 (16.75)
Multi-agent, *n (%)*	38 (19.9)
Not received, *n (%)*	7 (3.66)
Chemotherapy ≥4 months	
Yes, *n (%)*	94 (49.21)
No/not received, *n (%)*	97 (47.12)
ECOG performance status score (0-5)	
0, *n (%)*	75 (39.27)
1, *n (%)*	110 (57.59)
2, *n (%)*	6 (3.14)
>2, *n (%)*	0
Baseline CA19-9 ≥90 U/ml	
Yes, *n (%)*	110 (63.22)
No, *n (%)*	64 (36.78)
Pre-SBRT CA19-9 ≥90 U/ml	
Yes, *n (%)*	62 (33.16)
No, *n (%)*	125 (66.84)
Resected	
Yes, *n (%)*	103 (53.93)
No, *n (%)*	88 (46.07)
Margin-negative resection	
Yes, *n (%)*	87 (45.55)
No/not resected, *n (%)*	104 (54.45)

CA19-9, carbohydrate antigen 19-9; ECOG, Eastern Cooperative Oncology Group; SBRT, stereotactic body radiation therapy; SD, standard deviation

Table 2   Tumor and treatment characteristics by LA and BR stage

Parameters	LA (n = 128)	BR (n = 63)	P-value
Dosimetric			
GTV_D95, *mean (SD)*	33.99 (3.62)	33.06 (3.39)	*.09*
GTV_volume, *mean (SD)*	51.24 (34.56)	35.14 (22.19)	***<.01***
Shape relationship			
d_{SMA}, *mean (SD)*	−0.32 (0.75)	0.22 (0.88)	***<.01***
d_{CA}, *mean (SD)*	0.32 (1.48)	1.21 (1.51)	***<.01***
d_{CHA}, *mean (SD)*	0.22 (1.30)	0.84 (1.37)	***<.01***
$d_{CA,SMA}^{min}$, *mean (SD)*	−0.50 (0.75)	0.11 (0.89)	***<.01***
$d_{CA,SMA,CHA}^{min}$, *mean (SD)*	−0.56 (0.74)	0.00 (0.92)	***<.01***

BR, borderline resectable; dCA, distance between gross tumor volume and celiac axis; dCHA, distance between gross tumor volume and common hepatic artery; dSMA, distance between gross tumor volume and superior mesenteric artery; GTV, gross tumor volume; GTV_D95, dose that covers 95% of gross target volume; LA, locally advanced; min, minimum; SD, standard deviation
Italic bold, p<0.05
Italic, 0.05<p<0.10

Table 3 presents patient, tumor, and treatment characteristics, stratified by whether patients were able to undergo margin negative resection after SBRT. Compared with patients with unresected tumors, patients who were able to undergo resection had tumors that were significantly further from the SMA ($P < .01$). Patients who underwent resection trended toward tumors that were further from the CA and CHA but this was not significant ($P = .08$ and $P = .05$, respectively). Patients who underwent margin negative also were younger ($P < .01$), had smaller tumors ($P < .01$), underwent treatment more recently ($P < .01$), more commonly received multi-agent chemotherapy regimen ($P < .01$), more commonly received chemotherapy for ≥4 months ($P < .01$), and had lower baseline and pre-SBRT CA19-9 levels (both $P < .01$).

The decision tree (Fig 1) demonstrates that the most important factor that predicted margin negative resection was pre-SBRT chemotherapy regimen. Specifically, patients who received single-agent gemcitabine or did not receive neoadjuvant chemotherapy were far less likely to undergo a margin negative resection (12% vs 88%). Among patients who received multi-agent chemotherapy, arterial involvement was the next most important predictor as captured by $d_{CA,SMA,CHA}^{min}$. Specifically, if the tumor involved >1 cm of any of the key arterial structures, the patient was less likely to undergo margin negative resection (23% vs 77%).

However, if the tumor did not involve >1 cm of any of the 3 key arteries, the next critical predictive factor was age, with the model indicating 73 years of age as a cutoff. Among elderly patients (age ≥73 years) without >1 cm of arterial involvement, the most important predictive factor was the presence of arterial abutment of the CA or SMA. The presence of abutment within this subset suggested a low likelihood of margin-negative resection (n = 13; 23%), and a lack of abutment suggested a higher chance of margin-negative resection (n = 8; 68%). Interestingly, among younger patients (age <73 years) without >1 cm of arterial involvement, radiation dose was a key factor in predicting margin negative resectability. Within this subset, GTV D95 <26 Gy predicted a low likelihood of surgical resection (n = 12; 42%), and those with GTV D95 ≥26 Gy had a 75% chance of resection (n = 85).

The area under the curve for the decision tree was 0.66. Table 4 compares the decision tree model with NCCN staging in the prediction of resectability in our patient population. Among 63 patients with BR disease, 63% underwent margin negative resection, and among 128 patients with LA disease, 36% underwent resection. On the other hand, the decision tree model detected 29 additional patients who were classified as LA but successfully underwent surgery, which resulted in a higher sensitivity (79% vs 46%). Notably, the decision tree model showed comparative specificity (77% vs 78%). Overall, the decision tree model improved prediction accuracy compared with the NCCN guidelines (75% vs 63%; $P < .05$).

Of note, upfront systemic therapy is a well-accepted standard of care for patients with BR or LA disease; therefore, we performed an exploratory analysis that limited the model to patients who underwent at least 4 months of neoadjuvant systemic therapy (n = 94). As shown in Figure 2, the findings remained similar for arterial involvement, chemotherapy regimen, age, and radiation dose driving outcomes, but arterial involvement was higher up in the decision tree compared with chemotherapy regimen. Prediction accuracy remained improved compared with the standard NCCN guidelines (Suppl. Table 1).

Discussion

In patients with PC that involves local vasculature, prediction of resectability remains a challenge. The heterogeneity in outcomes within the current definitions of

Table 3 Patient, tumor, and treatment characteristics by margin negative status

Parameters	No (n = 104)	Yes (n = 87)	P-value
Dosimetric			
GTV_D95, *mean (SD)*	31.23 (2.96)	31.61 (2.49)	*.08*
GTV_volume, *mean (SD)*	54.63 (35.68)	36.73 (21.61)	*<.01*
Shape relationship			
d_{SMA}, *mean (SD)*	−0.29 (0.78)	0.04 (0.87)	*<.01*
d_{CA}, *mean (SD)*	0.42 (1.49)	0.86 (1.59)	*.08*
d_{CHA}, *mean (SD)*	0.27 (1.35)	0.62 (1.35)	**.05**
$d_{CA,SMA}^{min}$, *mean (SD)*	−0.47 (0.78)	−0.1 (0.89)	*<.01*
$d_{CA,SMA,CHA}^{min}$, *mean (SD)*	−0.57 (0.76)	−0.13 (0.89)	*<.01*
Other			
Age	66.52 (10.094)	62.39 (9.14)	*<.01*
Sex			.62
Male	52	46	
Female	52	41	
Race			.93
White	88	74	
Other	16	13	
Tumor location			.24
Head	69	53	
Body	33	27	
Tail	1	5	
Other	1	2	
Treatment year			*<.01*
2010-2012	28	7	
2013	15	13	
2014	22	25	
2015	31	34	
2016	6	10	
ECOG performance status score (0-5)			.30
0	42	33	
1	57	53	
2	5	1	
>2	0	0	
Chemotherapy regimen			*<.01*
Gemcitabine alone	31	5	
FOLFIRINOX	33	45	
Gemcitabine/nab-paclitaxel,	16	16	
Multi-agent	17	21	
None	7	0	
Chemotherapy ≥4 months			*<.01*
Yes	44	50	
No	60	37	
Pre-SBRT CA19-9 ≥90 U/ml			*<.01*
Yes	45	17	
No	56	69	
Baseline CA19-9 ≥90 U/ml			*<.01*
Yes	73	37	
No	26	38	

CA19-9, carbohydrate antigen 19-9; BR, borderline resectable; ECOG, Eastern Cooperative Oncology Group; dCA, distance between gross tumor volume and celiac axis; dCHA, distance between gross tumor volume and common hepatic artery; dSMA, distance between gross tumor volume and superior mesenteric artery; GTV, gross tumor volume; GTV_D95, dose that covers 95% of gross target volume; LA, locally advanced; min, minimum; SBRT, stereotactic body radiation therapy; SD, standard deviation

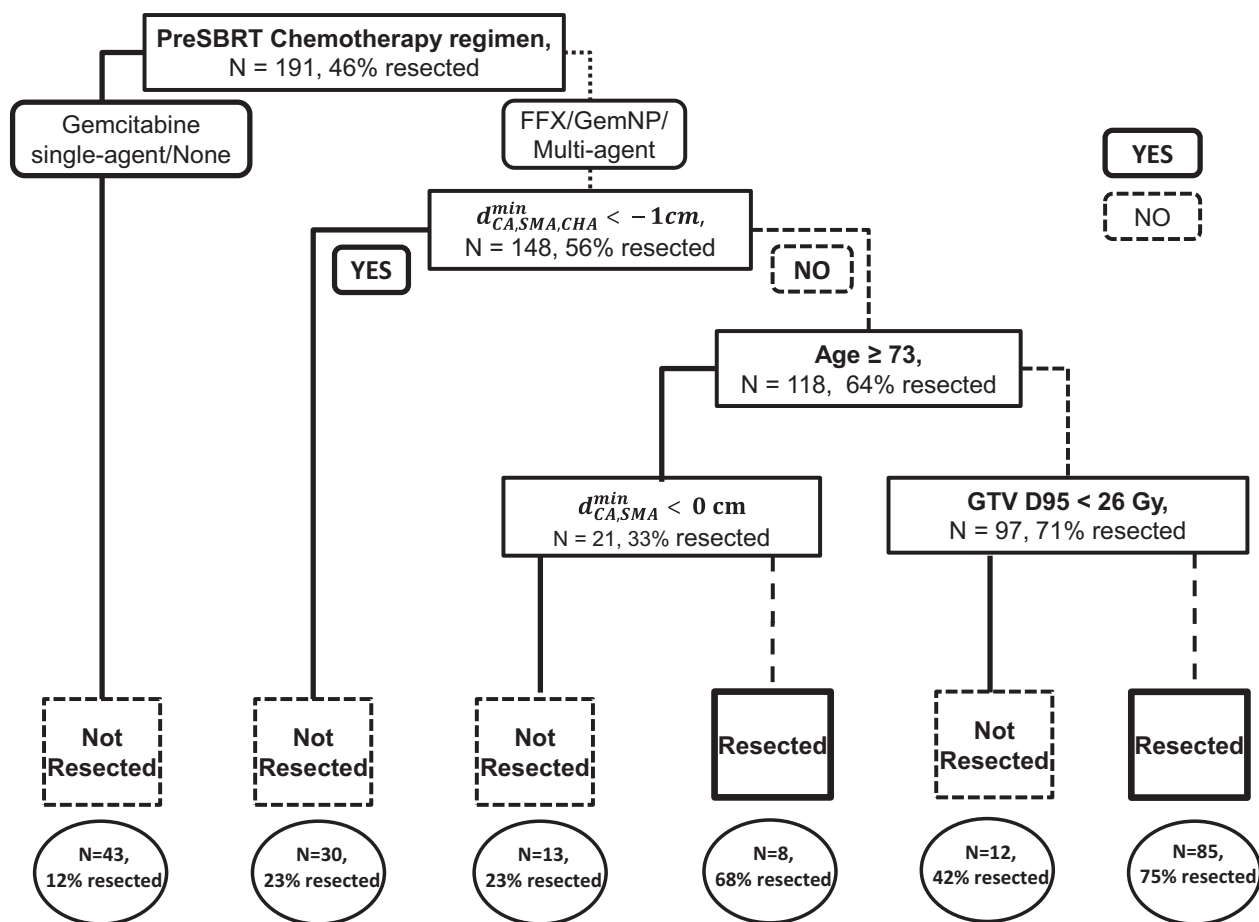Italian bold, p<0.05

Italian, 0.05<p<0.10

Figure 1 Decision tree for margin negative resectability among patients with initial locally advanced and borderline resectable pancreatic cancer. Nodes display the predicting factors and partitioning points. The potential risk factors in the Classification and Regression Trees analysis were chemotherapy regimen, closest distance between gross tumor volume (GTV) to any of superior mesenteric artery, celiac axis, and common hepatic artery, patient age, closest distance between GTV and superior mesenteric artery or celiac axis and GTV D95.

BR and LA disease highlights the need for more accurate models to predict surgical candidacy and support informed treatment decisions.[3,9–11] As such, we applied an exploratory approach to identify the most important predictors for resectability in patients undergoing neo-adjuvant chemotherapy and SBRT.

Table 4 Comparison of resectability predictions between physicians by NCCN guideline staging and CART model

NCCN guideline	Margin negative resection			Model prediction before SBRT	Margin negative resection		
	Yes	No	Total		Yes	No	Total
Yes	40	23	63	Yes	69	24	93
No	47	81	128	No	18	80	98
Total	87	104	191	Total	87	104	191

CART, Classification and Regression Trees; NCCN, National Comprehensive Care Network; SBRT, stereotactic body radiation therapy

Our analysis revealed multiple interesting findings. First, we show the ability to use OVH analysis to characterize the relationship between tumor and vasculature in a continuous manner compared with more commonly used categorical descriptions such as abutment or encasement. Using OVH-driven measures of vascular involvement, we found that a consideration of the highest degree of arterial involvement among the 3 key arterial structures was more important than examining the involvement of individual arteries. Among individual arteries, however, SMA involvement was more intimately associated with margin-negative resection compared with CA and CHA involvement, which trended toward significance. The reason for this difference between arteries in their association with resection merits further investigation. Possible explanations include the fact that celiac resection can potentially be an option through an Appleby procedure but involvement of the CHA may often represent lymph node disease that is easier to dissect.[29,30]

More importantly, our model showed the importance of both patient and treatment factors in dictating
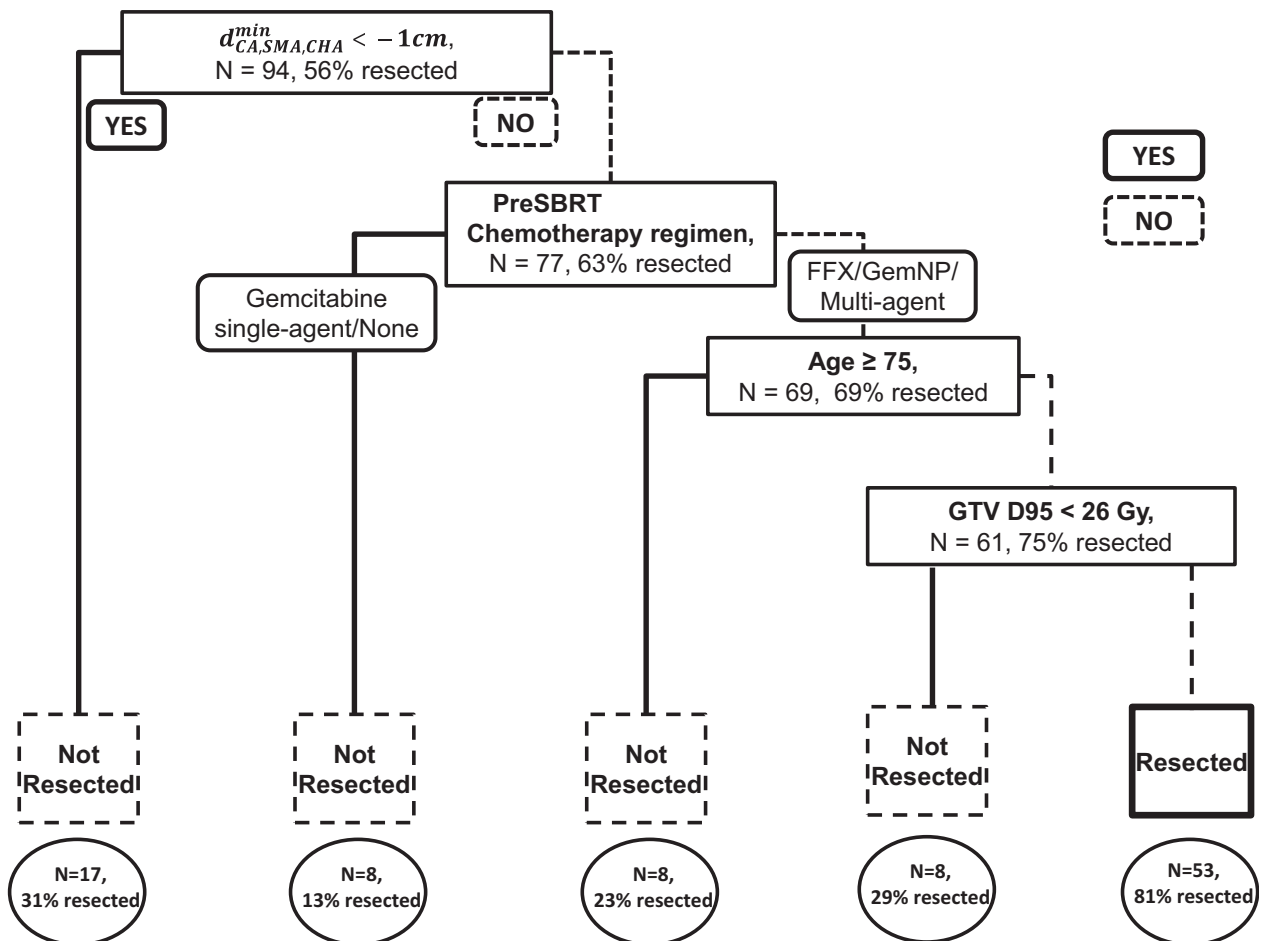
Figure 2   Decision tree for margin negative resectability among patients with initial locally advanced and borderline resectable prostate cancer who received more than 4 months of chemotherapy. Nodes display the predicting factors and partitioning points. The potential risk factors in the Classification and Regression Trees analysis were the closest distance between gross tumor volume (GTV) to any of superior mesenteric artery, celiac axis, and common hepatic artery, chemotherapy regimen, patient age, closet distance between GTV and superior mesenteric artery or celiac axis and GTV D95.

outcomes. Specifically, chemotherapy regimen and duration both played an important role in resectability, as well as age. Certainly, these findings match the anecdotal experience at our institution in which our surgeons are willing to explore patients with significant vascular involvement if they are younger and healthier and have undergone a long trial of intensive systemic therapy.[31] Future analysis that incorporates comorbidity would likely be further beneficial.

Perhaps more interesting was the importance of radiation dose and coverage in influencing surgical outcome. Indeed, this association supports further investigation into dose escalation in this population and may also have implications on treatment planning evaluation.[32-35] Perhaps most interesting was the lack of importance of NCCN staging, which did not appear in the decision tree and was supplanted by the aforementioned variables. Indeed, compared with the model, the NCCN definitions of BR and LA disease performed less in predicting

surgical resectability, which highlights the limitations of the current staging guidelines.

A number of limitations of this study must be acknowledged. First and foremost, this model is specific to patients who were treated in accordance with our institutional practice patterns, which generally consists of neoadjuvant chemotherapy and SBRT for patients with BR or LA disease. Nevertheless, considerable amounts of data now support such an approach, which is becoming increasingly common and incorporated into national trial designs.[36-38] Certainly, CART modeling is subject to model unstableness and overfitting. However, we used leave-one-out cross-validation to balance the recursive partitioning (branching) and pruning to overcome the potential instability in model development. We used CART because of its self-explanatory nature and because CART lends itself to a graphical representation in a decision-tree format that facilitates interpretation. This allows for an easy applicability of the predictive model in

clinical practice to distinguish between surgical and non-surgical candidates and guide personalized management decisions.

Another limitation is that venous involvement was not included in the model. Given the potential for reconstruction, venous involvement generally drives surgical decision-making at our institution less so than arterial involvement, but nonetheless should be incorporated into future studies. The future direction of research should also evaluate whether higher doses are associated with higher chances of resectability, perhaps through collaborative efforts using propensity-matching frameworks, which could result in more refined models.

Lastly, we used anatomy data derived from our simulation CT at the time of SBRT rather than a diagnostic CT at the time of diagnosis. However, our study focuses on the prediction of resectability before SBRT to support decisions at this time point such as modification of the treatment intent or plan. Nevertheless, future analyses at multiple time points throughout the neoadjuvant treatment course and using higher-resolution, diagnostic, pancreas-protocol CT would be worthwhile.

Conclusions

We developed a model that improved the prediction of margin-negative resectability compared with the standard NCCN guidelines in a population of patients at our institution with BR and LA PC. Our model included a continuous measure of arterial involvement and also highlighted the importance of patient and treatment characteristics, such as age, chemotherapy regimen and duration, and radiation dose and coverage, the latter of which may provide a rationale for radiation dose escalation.

These findings are hypothesis generating and need to be validated in external datasets, but illustrate the potential for advanced modeling in this sphere. Hopefully, this study encourages collaborative efforts that result in more refined models, which can help guide the care of patients with PC.

Supplementary data

Supplementary material for this article (https://dx.doi.org/10.1016/j.adro.2018.07.002) can be found at advanceradonc.org.

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