

eliminate abnormal growth in the pancreas because adiponectin has been reported to inhibit tumor cell growth and induce apoptosis (15).

The finding by Bao et al. of an association between adiponectin and pancreatic cancer has both mechanistic and translational potential. Firmly establishing a link between adiponectin levels and pancreatic cancer risk will suggest that glucose/fat metabolism contributes to the pathophysiology of pancreatic cancer. Future studies in this direction are expected to help us better understand the molecular events that are responsible for pancreatic cancer tumorigenesis. Further studies on issues such as the dynamic changes of high/low-molecular-weight adiponectin levels during the development of pancreatic cancer can yield key information to determine whether plasma adiponectin levels could be used as a predictive biomarker. Currently, most cases of pancreatic cancer are diagnosed at a late stage, contributing to high mortality rates. Adiponectin assessment may be used to prescreen patients with metabolic disorders such as diabetes for the detection of pancreatic cancer at an early stage. Early detection by the assessment of adiponectin has the potential to improve the survival rates of pancreatic tumor patients. It is also inviting to speculate that therapeutic interventions to increase the levels of circulating adiponectin may prevent the development of pancreatic cancer and/or improve the survival of patients with malignancy.

## References

1. Bao Y, Giovannucci EL, Kraft P, et al. XXX. *J Natl Cancer Inst*. In press.
2. Ben Q, Xu M, Ning X, Liu J, Hong S, Huang W, et al. Diabetes mellitus and risk of pancreatic cancer: a meta-analysis of cohort studies. *Eur J Cancer*. 2011;47(13):1928–1937.
3. Bartosch-Harlid A, Andersson R. Diabetes mellitus in pancreatic cancer and the need for diagnosis of asymptomatic disease. *Pancreatol*. 2010;10(4):423–428.
4. Hivert MF, Sullivan LM, Shrader P, Fox CS, Nathan DM, D'Agostino RB, Sr, et al. Insulin resistance influences the association of adiponectin levels with diabetes incidence in two population-based cohorts: the Cooperative Health Research in the Region of Augsburg (KORA) S4/F4 study and the Framingham Offspring Study. *Diabetologia*. 2011;54(5):1019–1024.
5. Miyoshi Y, Funahashi T, Kihara S, Taguchi T, Tamaki Y, Matsuzawa Y, et al. Association of serum adiponectin levels with breast cancer risk. *Clin Cancer Res*. 2003;9(15):5699–5704.
6. Hofmann JN, Liao LM, Pollak MN, Wang Y, Pfeiffer RM, Baris D, et al. A prospective study of circulating adipokine levels and risk of multiple myeloma. *Blood*. 2012;120(22):4418–4420.
7. Stolzenberg-Solomon RZ, Weinstein S, Pollak M, Tao Y, Taylor PR, Virtamo J, et al. Prediagnostic adiponectin concentrations and pancreatic cancer risk in male smokers. *Am J Epidemiol*. 2008;168(9):1047–1055.
8. Grote VA, Rohrmann S, Dossus L, Nieters A, Halkjaer J, Tjonneland A, et al. The association of circulating adiponectin levels with pancreatic cancer risk: a study within the prospective EPIC cohort. *Int J Cancer*. 2012;130(10):2428–2437.
9. Chang MC, Chang YT, Su TC, Yang WS, Chen CL, Tien YW, et al. Adiponectin as a potential differential marker to distinguish pancreatic cancer and chronic pancreatitis. *Pancreas*. 2007;35(1):16–21.
10. Kim JY, van de Wall E, Laplante M, Azzara A, Trujillo ME, Hofmann SM, et al. Obesity-associated improvements in metabolic profile through expansion of adipose tissue. *J Clin Invest*. 2007;117(9):2621–2637.
11. Yamauchi T, Kamon J, Ito Y, Tsuchida A, Yokomizo T, Kita S, et al. Cloning of adiponectin receptors that mediate antidiabetic metabolic effects. *Nature*. 2003;423(6941):762–769.
12. Jalovaara K, Santaniemi M, Timonen M, Jokelainen J, Kesaniemi YA, Ukkola O, et al. Low serum adiponectin level as a predictor of impaired glucose regulation and type 2 diabetes mellitus in a middle-aged Finnish population. *Metabolism*. 2008;57(8):1130–1134.
13. Oh DK, Ciaraldi T, Henry RR. Adiponectin in health and disease. *Diabetes Obes Metab*. 2007;9(3):282–289.
14. Rizza S, Gigli F, Galli A, Michelini B, Lauro D, Lauro R, et al. Adiponectin isoforms in elderly patients with or without coronary artery disease. *J Am Geriatr Soc*. 2010;58(4):702–706.
15. Cong L, Gasser J, Zhao J, Yang B, Li F, Zhao AZ. Human adiponectin inhibits cell growth and induces apoptosis in human endometrial carcinoma cells, HEC-1-A and RL95 2. *Endocr Rel Cancer*. 2007;14(3):713–720.

**Affiliation of authors:** Department of Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY (JZ, SNH).

DOI:10.1093/jnci/djs524

Advance Access publication December 21, 2012

©The Author 2012. Published by Oxford University Press. All rights reserved. For Permissions, please e-mail: journals.permissions@oup.com.

## Treatment for Breast Cancer: Is Time Really of the Essence?

Priscilla F. McAuliffe, Sandra Danoff, Steven D. Shapiro, Nancy E. Davidson

**Correspondence to:** Nancy E. Davidson, University of Pittsburgh Cancer Institute and UPMC CancerCenter, 5150 Centre Ave, Ste 500, Pittsburgh, PA 15213 (e-mail: davidsonne@upmc.edu).

It is accepted for breast cancer that early detection and prompt treatment lead to better outcome. In this issue of the Journal, Vandergrift et al. (1) evaluate the time interval between breast cancer diagnosis and initiation of adjuvant chemotherapy after definitive surgery to identify patient demographic and clinical features that might be actionable variables to decrease treatment delays. Using the National Comprehensive Cancer Network (NCCN) outcomes database, mean time to chemotherapy for 6622 patients diagnosed with stage I to stage III breast cancer between 2003 and 2009 and treated at nine participating NCCN cancer centers was

12 weeks and increased monotonically from 10.8 weeks in 2003 to 13.3 weeks in 2009. Increased utilization of diagnostic testing such as the 21-gene reverse transcription polymerase chain reaction assay and breast magnetic resonance imaging (MRI) appeared to strongly contribute to this increase. Not surprisingly, multiple surgical excisions and postmastectomy reconstruction also delayed adjuvant chemotherapy. Finally, increasing age and comorbidities, lower socioeconomic status, and transfer of care to an NCCN cancer center after diagnosis, particularly for black women with Medicaid insurance, were associated with increased time to chemotherapy.

The strengths of this retrospective study include the large patient cohort and the contemporary analysis that incorporated recent additions in our breast cancer diagnosis and treatment algorithms. But the decision to evaluate this modern patient cohort came at the price of availability of outcome data. Also, patients receiving preoperative chemotherapy and those with distant disease were excluded from this cohort that includes only patients with operable cancers. Last, all patients were treated at NCCN institutions, and it could be argued that these results may not be representative of breast cancer care across the United States, most of which is delivered in nonacademic medical centers. However, there is evidence to suggest that both academic and community sites provide appropriate breast cancer care (2).

Because accelerated treatment of breast cancer is thought to be a critical factor in patient survival, for many years women underwent a “one step” operation of excisional biopsy, intraoperative pathologic assessment, and mastectomy, and they would emerge from anesthesia to discover their diagnosis and surgical outcome. There was ultimately strong consensus that this is far from ideal, and the approach was abandoned. So what is the clinical impact of a 13-week time interval between diagnosis and adjuvant chemotherapy? Most recent, prospective, randomized, phase III trials that evaluated adjuvant systemic chemotherapy regimens specifically define an acceptable time period between definitive surgery and chemotherapy for patient enrollment eligibility to be generally not more than 12 weeks (3,4). Not surprisingly, no randomized trials have specifically addressed the effect of timing of initiation of adjuvant chemotherapy for breast cancer outcome. The results of retrospective studies evaluating this variable suggest that the impact of this parameter, if any, is limited (5). Although patients with estrogen receptor–negative breast cancer were found to have a worse prognosis with longer time to initiation of cyclophosphamide, methotrexate, and fluorouracil chemotherapy in one study (6), this was not confirmed when timing of anthracycline-based adjuvant chemotherapy was evaluated (7). The current study describes an average 12-week delay from diagnosis to chemotherapy, whereas the handful of studies that do indicate worsened prognosis described a much longer delay from definitive surgery to chemotherapy, a delay and ensuing poor outcome that may be confounded by patients’ overall health (8,9).

Even if this delay appears not to affect patients medically, might it affect them socially, psychologically, and economically? Does the delay worsen anxiety? Or does it allow a “time-out” to consider treatment options? Does it give patients the opportunity to adjust to alterations in their health and body image that can occur with diagnosis of breast cancer? Does it allow them to make better arrangements at work or at home? These are unanswered questions.

What can we as health-care providers do to reduce this interval? That the largest effect on time to chemotherapy was due to surgical reexcision and postmastectomy reconstruction bears careful reflection. Reexcisions burden patients with inconvenience, cost, discomfort, decreased cosmesis, and psychological stress, and they often lead to mastectomy that may then require reconstruction. The controversy about what constitutes a negative surgical margin remains heated (10). Several of the earliest trials establishing the efficacy of breast-conserving surgery with radiation required only macroscopic tumor removal, and microscopic margins were

either not assessed or defined as “no ink on tumor” (11,12). It is not proven that a larger negative margin decreases risk of local recurrence. Rather, it is likely that underlying tumor biology (13,14) and effective modern adjuvant therapy (15,16) play a larger role in determining this risk. A consensus on the definition of negative margins might allow more selective use of reexcision and decrease resultant mastectomies, thereby reducing time to chemotherapy.

The prolongation of time to chemotherapy due to use of diagnostic breast MRI also deserves mention (17). No randomized, controlled trial has shown reduction in local recurrence with the addition of MRI to the evaluation of patients with breast cancer. However, performing MRI leads to conversion from lumpectomy to mastectomy approximately 20% of the time (18,19). Did the MRI, which clearly delayed time to chemotherapy, truly improve breast cancer outcome or simply move the surgical management needlessly away from breast conservation? Although MRI does detect a contralateral breast cancer in 3% of patients (20), it is unclear whether systemic treatment of the index cancer would have treated the clinically occult contralateral cancer.

In addition to delays caused by additional testing or procedures, slow transfer of care and long wait time to schedule appointments with appropriate specialists may be untapped opportunities for intervention to improve care efficiency. At the University of Pittsburgh Medical Center (UPMC), we have successfully implemented an institution-wide 72-hour access policy, such that all symptomatic, nonurgent patients are offered an appropriate appointment within 72 hours. A 72-hour window was selected because internal review demonstrated that cancellations and missed appointments doubled if the time between scheduling and the appointment exceeded this. Before this initiative began in 2002, only 17% of patients were given such a timely appointment. Each of the 32 subspecialty services, comprising 1900 physicians, as well as community practices at UPMC, were given latitude and flexibility to determine how to achieve the 72-hour benchmark, according to their unique needs. Within our breast center, initiatives included establishing same-day postoperative medical oncology consultations, streamlining urgent genetic counseling, using physician extenders, creating a Wellness Clinic for patients in long-term follow-up, centralizing scheduling, and launching a patient navigator program charged with identifying patient populations with additional barriers to care. Changes initiated by other specialties to meet the benchmark included use of a physician-of-the-day model or more generalists. Within 1 year, 75% of the services were in compliance. Today compliance is nearly 100% and is monitored biweekly using trained “standardized patient” callers. These provider-driven interventions have significantly decreased time to treatment and greatly improved the patient experience. The success of and compliance with the UPMC 72-hour access initiative shows that implementing such measures to minimize inefficient transfers in care is possible in a large and complex health system.

In sum, the Vandergrift et al. (1) study shows that several patient, treatment, and systems factors contribute to time from breast cancer diagnosis to adjuvant chemotherapy. Initiatives to improve transfers in care and optimize definition of surgical margins, as well as thoughtful use of imaging, are within our control and should be pursued. However, some of these “delays,” such as moving to a “two stage” procedure or the use of the OncotypeDX assay, have greatly improved patient care. This suggests that

we should proceed with caution before using time to initiation of treatment as a quality measure for breast cancer treatment (21,22). Evaluating time to treatment outside of the context of outcomes cannot accurately access quality. Indeed, faster is not always better.

## References

1. Vandergrift JL, Niland JC, Theriault RL, et al. Time to adjuvant chemotherapy for breast cancer in National Comprehensive Cancer Network (NCCN) institutions. *J Natl Cancer Inst.* 2013;105(2):XXXX-XXXX.
2. In H, Neville BA, Lipsitz SR, et al. The role of National Cancer Institute-designated cancer center status: observed variation in surgical care depends on the level of evidence. *Ann Surg.* 2012;255:890-895.
3. Bonadonna G, Valagussa P, Moliterni A, et al. Adjuvant cyclophosphamide, methotrexate, and fluorouracil in node-positive breast cancer: the results of 20 years of follow-up. *N Engl J Med.* 1995;332:901-906.
4. Levine MN, Bramwell VH, Pritchard KI, et al. Randomized trial of intensive cyclophosphamide, epirubicin, and fluorouracil chemotherapy compared with cyclophosphamide, methotrexate, and fluorouracil in premenopausal women with node-positive breast cancer. National Cancer Institute of Canada Clinical Trials Group. *J Clin Oncol.* 1998;16:2651-2658.
5. Buzdar AU, Smith TL, Powell KC, et al. Effect of timing of initiation of adjuvant chemotherapy on disease-free survival in breast cancer. *Breast Cancer Res Treat.* 1982;2:163-169.
6. Colleoni M, Bonetti M, Coates AS, et al. Early start of adjuvant chemotherapy may improve treatment outcome for premenopausal breast cancer patients with tumors not expressing estrogen receptors. The International Breast Cancer Study Group. *J Clin Oncol.* 2000;18:584-590.
7. Shannon C, Ashley S, Smith IE. Does timing of adjuvant chemotherapy for early breast cancer influence survival? *J Clin Oncol.* 2003;21:3792-3797.
8. Lohrisch C, Paltiel C, Gelmon K, et al. Impact on survival of time from definitive surgery to initiation of adjuvant chemotherapy for early-stage breast cancer. *J Clin Oncol.* 2006;24:4888-4894.
9. Cold S, Durning M, Ewertz M, et al. Does timing of adjuvant chemotherapy influence the prognosis after early breast cancer? Results of the Danish Breast Cancer Cooperative Group (DBCG). *Br J Cancer.* 2005;93:627-632.
10. Morrow M, Harris JR, Schnitt SJ. Surgical margins in lumpectomy for breast cancer—bigger is not better. *N Engl J Med.* 2012;367:79-82.
11. Veronesi U, Cascinelli N, Mariani L, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. *N Engl J Med.* 2002;347:1227-1232.
12. van Dongen JA, Voogd AC, Fentiman IS, et al. Long-term results of a randomized trial comparing breast-conserving therapy with mastectomy: European Organization for Research and Treatment of Cancer 10801 trial. *J Natl Cancer Inst.* 2000;92:1143-1150.
13. Mamounas EP, Tang G, Fisher B, et al. Association between the 21-gene recurrence score assay and risk of locoregional recurrence in node-negative, estrogen receptor-positive breast cancer: results from NSABP B-14 and NSABP B-20. *J Clin Oncol.* 2010;28:1677-1683.
14. Ho AY, Gupta G, King TA, et al. Favorable prognosis in patients with T1a/T1bN0 triple-negative breast cancers treated with multimodality therapy. *Cancer.* 2012;118:4944-4952.
15. Fisher B, Dignam J, Bryant J, et al. Five versus more than five years of tamoxifen therapy for breast cancer patients with negative lymph nodes and estrogen receptor-positive tumors. *J Natl Cancer Inst.* 1996;88:1529-1542.
16. Romond EH, Perez EA, Bryant J, et al. Trastuzumab plus adjuvant chemotherapy for operable HER2-positive breast cancer. *N Engl J Med.* 2005;353:1673-1684.
17. Fisher B. Role of science in the treatment of breast cancer when tumor multicentricity is present. *J Natl Cancer Inst.* 2011;103:1292-1298.
18. Berg WA, Gutierrez L, Ness-Aiver MS, et al. Diagnostic accuracy of mammography, clinical examination, US, and MR imaging in preoperative assessment of breast cancer. *Radiology.* 2004;233:830-849.
19. Bedrosian I, Mick R, Orel SG, et al. Changes in the surgical management of patients with breast carcinoma based on preoperative magnetic resonance imaging. *Cancer.* 2003;98:468-473.
20. Lehman CD, Gatsonis C, Kuhl CK, et al. MRI evaluation of the contralateral breast in women with recently diagnosed breast cancer. *N Engl J Med.* 2007;356:1295-1303.
21. McCahill LE, Privette A, James T, et al. Quality measures for breast cancer surgery: initial validation of feasibility and assessment of variation among surgeons. *Arch Surg.* 2009;144:455-462; discussion 462-463.
22. Desch CE, McNiff KK, Schneider EC, et al. American Society of Clinical Oncology/National Comprehensive Cancer Network quality measures. *J Clin Oncol.* 2008;26:3631-3637.

**Affiliations of authors:** University of Pittsburgh Cancer Institute, Pittsburgh, PA (PFM, SDS, NED); University of Pittsburgh Medical Center, Pittsburgh, PA (PFM, SDS, SD); UPMC CancerCenter, Pittsburgh, PA (NED).

DOI:10.1093/jnci/djs523

Advance Access publication December 28, 2012

©The Author 2012. Published by Oxford University Press. All rights reserved.  
For Permissions, please e-mail: journals.permissions@oup.com.

# Tumor Boards (Team Huddles) Aren't Enough to Reach the Goal

Douglas W. Blayney

**Correspondence to:** Douglas W. Blayney, MD, Stanford Cancer Institute, Stanford School of Medicine, 875 Blake Wilbur Dr, CC 2213, MC 5827, Stanford, CA 94305-5827 (e-mail: dblayney@stanford.edu).

It should be no surprise that improved performance on the process or outcome measures of quality is not predicted by the existence of team meetings. Anyone who has ever played a team sport, worked with a laboratory team, led a clinical trial team, or led a patient care team soon realizes that huddles, lab meetings, cooperative group meetings, or attending physician rounds don't get the job done. Huddles are a necessary but not sufficient feature of high-functioning teams. Execution of the plan is how we get to good outcomes

regardless of the brilliance of the plan, the talent of the team, or the difficulty of the task.

Contemporary cancer care is multidisciplinary. Tumor boards are team meetings of the multidisciplinary team. Typically, patients with newly diagnosed cancer are formally discussed by representatives of various cancer care specialties. Medical, surgical, and radiation oncologists, as well as pathologists and diagnostic imaging specialists, attend. Palliative care, social work and chaplaincy