Intensive or not surveillance of patients with colorectal cancer after curative resection

Gerardo Rosati

Abstract

It is common practice to follow patients with colorectal cancer for some years after resection and/or adjuvant treatment. Data are lacking about how often patients should be seen, what tests should be performed, and what surveillance strategy has a significant impact on patient outcome. Seven randomized trials have addressed this issue, but none had sufficient statistical power. Four published meta-analyses have established that overall survival is significantly improved for patients in the more intensive programs of follow-up. This improvement amounts to a risk difference of 7% (95% CI: 3%-12%, P = 0.002) in 5-year survival. This should be partly attributable to more frequent reoperation for cure of asymptomatic recurrence, or more intense follow-up, as well other factors, such increased psychosocial support and well-being, diet and lifestyle optimization, and/or improved treatment of coincidental diseases. A large-scale multicenter European study [Gruppo Italiano di Lavoro per la Diagnosi Anticipata (GILDA)] is underway to answer the question of what constitutes optimal surveillance for patients after primary therapy, based on an adequately powered study.

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OPEN QUESTIONS
An optimal level of follow-up would maximize patient welfare at the least cost. Patients are harmed if a strategy is too intensive, because they are unnecessarily exposed to radiation, and undergo uncomfortable endoscopy and blood tests. If high-intensity surveillance testing provides no improvement in duration or quality of life (QoL), society is also harmed by the waste of resources. If the strategy is not intensive enough, patients who relapse and are potential candidates for effective salvage treatment may die needlessly. Society is also harmed in this case because the costs to treat incurable CRC are high, patients are unable to work, their QoL decreases, and their children grow up without a parent[6]. How good is the evidence for choosing which follow-up examinations to order?

Early detection of CRC recurrence is seldom useful. In this context, intensive testing leads to anxiety and financial burden, and seldom changes disease outcomes. On the contrary, to wait for signs or symptoms, rather than detecting early disease manifestations is defensible, albeit somewhat paternalistic. Physical examination virtually never discards early hepatic, lung, or anastomotic recurrence, and CEA is only elevated in 60% of patients with recurrence. Thus, waiting for signs and symptoms seems contrary to the instinct that early detection and prompt disease management is best[6].

WHAT IS KNOWN ON THIS TOPIC?
In an attempt to rationalize care, the concept of the randomized trial was introduced in the mid-twentieth century. However, very few of these studies have dealt with follow-up of patients with CRC, and no consensus has been reached with respect to the most effective strategy. Indeed, follow-up schedules are highly heterogeneous with regard to procedures (clinical history, physical examination, CEA monitoring, imaging techniques, and colonoscopy) and the frequency with which they are carried out.

Seven randomized controlled trials have addressed this issue, but none had sufficient statistical power[9-13]. Thus, four meta-analyses have been published to evaluate the impact of various intensities and strategies on the outcome of patients after curative surgery for CRC[13-16]. Overall survival is significantly improved for patients in the more intensive programs of follow-up. This improvement amounts to a risk difference of 7% (95% CI: 3%-12%, P = 0.002) in 5-year survival[13]. The incidence of asymptomatic recurrence is significantly more common in patients in the more intensive follow-up program. This may explain the more frequent reoperation for recurrence in that group of patients.

The analysis of Renchen et al[13] has found a larger impact on survival in trials using abdominal CT and frequent CEA determinations. The study by Jeffery et al[16] had similar findings. The patients undergoing more intense follow-up have improved survival, earlier diagnosis of recurrence, and more frequent curative resection, as a result of undergoing more tests, especially liver imaging.

However, it is not clear to date which tests or frequency of visits is optimal. Also noted in these overviews are the paucity of data on complications and QoL.

One trial noted two perforations and two episodes of bleeding after polyectomy in 731 colonoscopies: a complication rate of 0.55%[9]. This complication rate is comparable to that of other colonoscopy studies[17].

The QoL and attitude of patients participating in follow-up programs have been investigated by Stiggelbout et al[18]. Their results have indicated that regular contact with a physician reassures patients, and that visits and tests cause only slight anticipatory anxiety and other minor inconveniences[18].

Kjeldsen et al[19] have confirmed these findings in a subgroup of patients participating in a randomized trial that compared minimal to regular follow-up, and which demonstrated similar survival for both follow-up regimens. Patients were mailed the questionnaire to complete at home. Ninety-one percent returned the completed questionnaires. QoL measures and attitudes were almost the same for patients in the minimal and intensive follow-up programs, which indicated that the extra tests or inconveniences were balanced by the more frequent reassurance of health.

Other authors have postulated that improved survival with intensive follow-up is not only due to salvage surgery offering a second chance of cure, but that an additional 4%-11% gain in survival may be attributable to other factors[19]. The following may be relevant: (1) increased psychosocial support and well-being; (2) cancer survivors tend to optimize their diet and lifestyle, although it is unclear whether these adjustments are self-motivated, or a direct consequence of health-care interventions; and (3) improved treatment of coincidental disease.

CONCLUSION
Many doubts about follow-up of CRC patients must be clarified and further well-designed studies with a sufficient number of patients must be carried out. The generation of high-quality evidence for the practice of cancer patient follow-up is an important priority for the medical community, although trials are expensive to mount and take a long time to complete. In this context, two trials of high- vs low-intensity follow-up for breast cancer have been carried out, which indicates that such trials are feasible[19]. Both employed a randomized two-arm design with a sample size of about 1500 patients. The same is likely to be necessary for trials of CRC patient follow-up; one such trial by Gruppo Italiano di Lavoro per la Diagnosi Anticipata (GILDA) completed patient recruitment in September 2006, and the results should be published during 2010. Major objectives of this study are: overall survival, better timing profile of diagnosis of recurrence, QoL, and program costs. It is hypothesized that the results of high- and low-intensity strategies will be equivalent, and it will answer the question of what constitutes optimal surveillance for patients after primary therapy, based on an adequately powered study.
REFERENCES

1 Pisani P, Parkin DM, Bray F, Ferlay J. Estimates of the worldwide mortality from 25 cancers in 1990. Int J Cancer 1999; 83: 18-29
2 Abulafi AM, Williams NS. Local recurrence of colorectal cancer: the problem, mechanisms, management and adjuvant therapy. Br J Surg 1994; 81: 7-19
3 Vernava AM 3rd, Longo WE, Virgo KS, Coplin MA, Wade TP, Johnson FE. Current follow-up strategies after resection of colon cancer. Results of a survey of members of the American Society of Colon and Rectal Surgeons. Dis Colon Rectum 1994; 37: 573-583
4 Johnson FE, Virgo KS, Fossati R. Follow-up for patients with colorectal cancer after curative-intent primary treatment. J Clin Oncol 2004; 22: 1363-1365
5 Goldberg RM. Intensive surveillance after stage II or III colorectal cancer: is it worth it? J Clin Oncol 2006; 24: 330-331
6 Kjeldsen BJ, Kronborg O, Fenger C, Jørgensen OD. A prospective randomized study of follow-up after radical surgery for colorectal cancer. Br J Surg 1997; 84: 666-669
7 Mäkelä JT, Laitinen SO, Kairaluoma MI. Five-year follow-up after radical surgery for colorectal cancer. Results of a prospective randomized trial. Arch Surg 1995; 130: 1062-1067
8 Ohlsson B, Breland U, Ekberg H, Graffner H, Tranberg KG. Follow-up after curative surgery for colorectal carcinoma. Randomized comparison with no follow-up. Dis Colon Rectum 1995; 38: 619-626
9 Schoemaker D, Black R, Giles L, Toulou J. Yearly colonoscopy, liver CT, and chest radiography do not influence 5-year survival of colorectal cancer patients. Gastroenterology 1998; 114: 7-14
10 Pietra N, Sarli L, Costi R, Ouchemi C, Gratterola M, Peracchia A. Role of follow-up in management of local recurrences of colorectal cancer: a prospective, randomized study. Dis Colon Rectum 1998; 41: 1127-1133
11 Secco GB, Fardelli R, Gianquinto D, Bonfante P, Baldi E, Ravera G, Derchi L, Ferraris R. Efficacy and cost of risk-adapted follow-up in patients after colorectal cancer surgery: a prospective, randomized and controlled trial. Eur J Surg Oncol 2002; 28: 418-423
12 Rodríguez-Muranta F, Saló J, Arcusa A, Boadas J, Pitol V, Bessa X, Batiste-Alentorn E, Lacy AM, Delgado S, Maurel J, Piqué JM, Castells A. Postoperative surveillance in patients with colorectal cancer who have undergone curative resection: a prospective, multicenter, randomized, controlled trial. J Clin Oncol 2006; 24: 386-393
13 Renehan AG, Egger M, Saunders MP, O'Dwyer ST. Impact on survival of intensive follow up after curative resection for colorectal cancer: systematic review and meta-analysis of randomised trials. BMJ 2002; 324: 813
14 Jeffery GM, Hickey BE, Hider P. Follow-up strategies for patients treated for non-metastatic colorectal cancer. Cochrane Database Syst Rev 2002; CD002200.
15 Figueredo A, Rumble RB, Maroun J, Earle CC, Cummings B, McLeod R, Zuraw L, Zwaal C. Follow-up of patients with curatively resected colorectal cancer: a practice guideline. BMC Cancer 2003; 3: 26.
16 Tjandra JJ, Chan MK. Follow-up after curative resection of colorectal cancer: a meta-analysis. Dis Colon Rectum 2007; 50: 1783-1799
17 Dominitz JA, Eisen GM, Baron TH, Goldstein JL, Hirota WK, Jacobson BC, Johanson JF, Leighton JA, Mallery JS, Raddawi HM, Vargo J 2nd, Waring JP, Panelli RD, Wheeler-Harbough J, Faigel DO. Complications of colonoscopy. Gastrointest Endosc 2003; 57: 441-445
18 Stiggelbout AM, de Haes JC, Vree R, van de Velde CJ, Bruijinckx CM, van Groningen K, Kievit J. Follow-up of colorectal cancer patients: quality of life and attitudes towards follow-up. Br J Cancer 1997; 75: 914-920
19 Renehan AG, Egger M, Saunders MP, O'Dwyer ST. Mechanisms of improved survival from intensive followup in colorectal cancer: a hypothesis. Br J Cancer 2005; 92: 430-433

Rosati G. Surveillance of colorectal cancer