Is Any Method of Vascular Control Superior in Hepatic Resection of Metastatic Cancers?

Longmire Clamping, Pringle Maneuver, and Total Vascular Isolation

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Hypothesis: Although control of the hepatic vascular pedicle is commonly used during hepatic resection, the optimal method of vascular control continues to be debated. The utility of total or selective vascular isolation, pedicle inflow occlusion, or the absence of vascular isolation during minor and major hepatectomy needs to be examined.

Design: Retrospective review of hepatic resections performed for either isolated colorectal or noncolorectal hepatic metastases.

Setting: The University of Chicago Hospitals, Chicago, Ill, a tertiary-care referral center.

Patients: One hundred forty-one patients who underwent hepatic resection for isolated metastatic liver disease were identified through The University of Chicago Hospitals Tumor Registry.

Main Outcome Measures: Intraoperative parameters, perioperative morbidity and mortality, and tumor recurrence.

Results: Four groups were compared with alternative methods of vascular management, including total vascular isolation, Longmire clamping, Pringle maneuver, or no vascular control. Tumor number and size were not significantly different between groups. Blood loss and transfusion requirements tended to be higher in the total vascular isolation group and were significantly higher compared with the Pringle group ($P=.06$) and the no vascular control group ($P=.04$), but this also correlated with a higher incidence of complexity of surgical resection. The highest incidence of postoperative complications occurred in the total vascular isolation group ($P<.05$). With similar permanent pathologic margins, the rates of intrahepatic recurrence were similar among all groups, with the no vascular control group having the lowest recurrence rate.

Conclusions: All methods of vascular control appeared equivalent with respect to limiting blood loss and transfusion requirements while providing adequate surgical margins. The highest rates of blood requirements and complications were noted in the total vascular isolation group, which corresponded to the highest incidence of complex resections. The Longmire clamp group incurred the lowest incidence of complications and resulted in identical surgical margins. The application of vascular control is beneficial to surgeons during hepatic resection, but the method of control should be selected based on the location and complexity of resection required and preference of the individual surgeon.

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Liver resection remains the only potential curative treatment for metastases isolated in the liver. Advances in the techniques of hepatic resection have dramatically evolved during the last 2 decades with a decline in perioperative morbidity and mortality.$^{1,2}$ Operative mortality has consistently been reported as 2% to 4% in most large modern series.$^{2,3}$ The improvement in operative outcome can be attributed to both anesthetic and critical care advances and the development of segmentally based surgical resection techniques.$^{3,4}$ Advances in the methods of vascular control and segmentally based surgical resections limit morbidity and mortality to postoperative complications unrelated to blood loss.

Traditionally, the principal cause of morbidity and mortality in hepatic resection was directly related to intraoperative bleeding.$^{5,6}$ In an attempt to address this issue, the technique of total vascular isolation (TVI), first reported in 1966 by Heaney et al,$^7$ was introduced and included concomitant occlusion of the supraceliac aorta. As described by Bismuth et al,$^8$ TVI included inflow and outflow occlusion without supraceliac occlusion. Emre et al$^9$ and Zografos et al$^{10}$ have most recently advocated the use of TVI but noted...
**PATIENTS AND METHODS**

The University of Chicago Hospitals Tumor Registry was retrospectively examined to identify patients who underwent hepatic resection for isolated metastatic lesions to the liver from January 1, 1984, to January 1, 2000. All patients underwent exploration and tumor resection with curative intent for either colorectal or noncolorectal hepatic metastases.

Surgical techniques used included a bilateral subcostal incision with, if necessary, a midline extension, with intraoperative ultrasonosonography systematically used after the liver was completely mobilized. The method of vascular isolation used was based on intraoperative assessment and location of tumor with respect to the vena cava and hepatic veins and individual surgeon preference. Total vascular isolation is obtained by suprarenalatic and infrahepatic veno cava clamping and hepatic vascular inflow occlusion by vascular clamping (Figure 1). Supraceliac aortic cross clamping has not been performed by our group; however, ligation of the right adrenal vein is frequently performed to complete the TVI. The use of renal dose dopamine hydrochloride is commonly used, whereas the administration of allopurinol or mannitol has not been used. Resection is carried out after test clamping for 5 to 10 minutes to determine patient stability. After transection, the infrahepatic inferior vena cava clamp is partially opened first to evacuate air and second to determine caval integrity. Longmire vascular clamping (Longmire) is performed by full mobilization of the lobe and placement of a parenchymal compression clamp. Selective ligation of the lobar portal vein hepatic artery and hepatic vein is performed if a lobar resection is to be performed. This technique is also amenable to peripheral wedge resections, which can be easily performed by minimizing the proportion of the liver placed within the Longmire clamp (Figure 2). Since unilateral ischemia is produced, no test clamping or preconditioning is required. Similar to the TVI group, dopamine is often used, whereas mannitol or allopurinol use is not advocated. Hepatic transection is performed by electrocautery followed by slow, graded vascular unclamping, requiring vascular suturing of the remaining bleeding sites. The Pringle maneuver (Pringle) is carried out by intermittent vascular occlusion of the afferent portal vein and hepatic artery. Lobar vessels are most frequently not isolated or divided during this method of vascular control (Figure 3). Intermittent occlusion is performed using umbilical tape, vascular clamp, or occlusive Penrose drain. In these patients, a 5- to 10-minute test clamp is performed to determine hemodynamic stability. If the patient is hemodynamically unstable, further volume loading is performed before additional vascular test clamping. Once inflow control has been achieved, the ischemic time is closely monitored. After inflow occlusion of 20 to 30 minutes, inflow is reestablished for a period of 10 minutes before reocclusion. Total ischemic time of less than 30 minutes is often all that is required; however, total ischemic time should remain at less than 60 minutes. No vascular control (NVC) was used principally for peripheral lesions during nonlobar resections. This technique includes parenchymal compression by the assistant surgeon. Fluid was drained from all patients with closed suction devices.

Clinical charts were retrospectively reviewed for patient demographics, symptoms, location of primary and metastatic disease, perioperative data, morbidity and mortality, and both overall and intrahepatic tumor recurrence. Long-term follow-up was obtained through hospital records, clinical charts, and telephone conversations with either primary care physicians or patients' families. All statistical evaluations were based on the date of patient's death or last follow-up.

All survival data are expressed as mean±SD unless otherwise indicated. The major end points of this study were intraoperative blood loss and transfusion requirements and perioperative morbidity and mortality. Intrahepatic tumor recurrence was also examined. All statistical evaluations were performed using the t test, χ² analysis, and Kaplan-Meier actuarial survival curves. Differences were considered statistically significant at P<.05.

**RESULTS**

From January 1, 1984, to January 1, 2000, 141 patients with either colorectal (n=110) or noncolorectal metastases (n=31) underwent surgical resection at The University of Chicago Hospitals. Four methods of vascular occlusion were used. The most common method of vascular control was the use of temporary inflow occlusion by the Pringle maneuver in 85 patients (60%). Total vascular isolation (20 [14%]) and Longmire clamping (21 [15%]) were used with similar frequency. The use of no vascular isolation was used infrequently for peripheral tumors in 15 patients (11%). The mean ages of patients undergoing resection in all groups were similar: Pringle group, 58.0±12.6 years; Longmire group, 61.6±9.7 years; TVI group, 59.4±13.1 years; and NVC group, 62.3±12.1 years (P=.5). Sex distribution was similar between all sub-
The incidence of noncolorectal metastases was highest in the Longmire group at 7 (35%) of 20, followed by the TVI group with 5 (24%) of 21, the NVC group at 3 (20%) of 15, and the Pringle group at 16 (19%) of 85 ($P = .6$). Metastatic tumor deposits were equivalent in all groups: NVC group, 2.0±1.5 lesions; Pringle group, 2.0±1.4 lesions; Longmire group, 1.9±1.6 lesions; and TVI group, 1.8±1.2 lesions ($P = .7$). Tumor size was smallest in the NVC group (3.8±2.2 cm), followed by the Longmire group (3.9±2.5 cm) and the Pringle group (5.1±3.7 cm), with the largest tumors located in the TVI patients (5.7±3.6 cm; $P = .5$). A comparison of the TVI group with the Longmire group showed a trend toward statistical significance ($P = .07$). Unilobar lesions predominated all groups; however, the highest incidence of bilobar lesions was noted in the TVI group (6 [29%] of 21) and the Pringle group (25 [29%] of 85). (The Longmire and NVC groups had incidences of 5 [25%] of 20 and 3 [20%] of 15 patients, respectively.) The NVC group consisted of the slowest growing tumors, with the time from a primary cancer resection to hepatic metastases of 38.1±61.1 months compared with 25.9±19.1 months in the Longmire group and 21.4±19.4 months in the TVI group ($P = .04$). The shortest interval was seen in the Pringle group, presenting 17.7±25.2 months after primary resection compared with the NVC group ($P = .03$).

Intraoperative blood loss was lowest in the NVC group (303.2±293.2 mL) followed by the Longmire group (572.5±1028.0 mL), Pringle group (625.9±637.2 mL), and TVI group (931.0±1122.6 mL). Blood loss in the TVI group was significantly higher than the NVC group ($P = .04$). Transfusions were most frequent in the TVI group at 1.3±3.4 units after primary resection compared with the NVC group ($P = .03$).

Figure 1. Application of total vascular isolation is obtained by cross clamping both the suprahepatic and infrahepatic vena cava, with hepatic vascular control of the portal vein and hepatic artery.

Figure 2. Longmire clamp control may be obtained either with or without ligation of the involved hepatic vein, portal vein, and hepatic artery branches. Application of the clamp is enabled by full mobilization of the hepatic lobe.

Length of hospital stay was shortest in the Longmire group at 5.6±1.5 days followed by the NVC group (7.5±3.1 days) and the TVI group (7.6±4.8 days). The longest hospital stay was noted in the Pringle group at 8.0±4.9 days. Postoperative complications were most frequent in the TVI group at 7 (33%) of 21 patients ($P = .04$), followed by the Pringle and NVC groups at a rate of 17 (20%) of 85 and 2 (13%) of 15 patients, respectively. The lowest incidence of postoperative complications was encountered in the Longmire group, with an incidence of 2 (10%) of 20 patients with 1 bile leak managed by interventional radiologic drainage and 1 postoperative respiratory arrest from oversedation without patient injury.

Overall tumor recurrence was lowest in the Longmire group at 4 (20%) of 20 patients compared with the Pringle (45 [53%] of 85), TVI (13 [62%] of 21), and NVC groups (7 [47%] of 15) ($P = .01$) (Figure 4). This sig-
nificantly lower recurrence rate may be an artifact of the mean shorter follow-up time of 16.6±12.9 months. This is a direct result of late introduction of this technique to our institution. Overall actuarial 1-year survival rate was similar for the Longmire group at 95% compared with the Pringle group (86%), TVI group (77%), and NVC group (86%). At the 3-year point, the Longmire group had a higher survival rate (95%), which was not statistically significant in comparison to the Pringle group (49%), TVI group (62%), and NVC group (40%), because of the short follow-up and small sample size. However, intrahepatic recurrence did not appear to be affected by the method of vascular control with recurrent hepatic disease noted in 12 (14%) of 85 patients in the Pringle group, 4 (20%) of 20 patients in the Longmire group, and 5 (24%) of 21 patients in the TVI group. The lowest incidence of intrahepatic recurrence was incurred in the NVC patients (2 [13%] of 15 patients). Similar disease-free survival figures were obtained at 1 and 3 years for the Longmire group (84% and 65%), TVI group (57% and 41%), Pringle group (64% and 33%), and NVC group (67% and 40%) (P = .5).

**COMMENT**

Hemorrhage has always been the principal concern during hepatic resection for benign or malignant lesions.\(^3,4\) This has led to the widespread use of portal triad clamping or more precise methods of vascular control, including selective and TVI of the liver to minimize hepatic bleeding during resection. The simplest method of hepatic resection is the manual compression of the hepatic tissue while the surgeon excises the tumor with an adequate margin. This method provides a reasonable approach for peripheral tumors of the liver; however, this method fails to provide adequate control for either nonperipheral or larger lesions that require more extensive liver resections. The Pringle maneuver allows hepatic pedicle inflow control but does result in global hepatic warm ischemia. The standard approach to hepatic warm ischemia during this method has been intermittent vascular clamping for 20- to 30-minute intervals with a total vascular clamping time of 60 minutes. This form of vascular control does decrease bleeding by diminishing portal and hepatic arterial inflow; however, the remaining uninvolved liver can be affected by the resulting hepatic ischemia or reperfusion injury. Patients with pre-existing liver conditions, including fatty infiltrate, fibrosis, or cirrhosis, can be most susceptible to ischemic injury. To approach more complex lesions located centrally, which require more extensive hepatic resections, the method of TVI was developed by Heaney et al,\(^7\) who first conceptualized the technique to involve supraceliac aortic control. This technique of aortic and venous control was thought to allow central resections in the proximity of major hepatic veins while reducing blood loss and risk of air embolism. Stephen et al\(^13\) later reported in their TVI experience that concomitant supraceliac aortic occlusion is beneficial not only in limiting blood loss, but also in providing hemodynamic stability and sparing splanchnic engorgement. Earlier groups incorporated in situ core cooling of the liver out of fear of normothermic ischemic injury.\(^14\) Huguet et al\(^15\) demonstrated that the human liver can tolerate warm ischemia for at least 60 minutes and perhaps as long as 90 min-

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**Postoperative Complications of Vascular Management Methods**

<table>
<thead>
<tr>
<th>Method and Complication</th>
<th>No. (%) of Patients With Complication</th>
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</thead>
<tbody>
<tr>
<td>Pringle maneuver</td>
<td>17/85 (20)</td>
</tr>
<tr>
<td>Abscess/bile leak</td>
<td>2</td>
</tr>
<tr>
<td>Infection</td>
<td>5</td>
</tr>
<tr>
<td>Reoperative bleeding</td>
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<tr>
<td>Pulmonary embolism</td>
<td>3</td>
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<tr>
<td>Death</td>
<td>1</td>
</tr>
<tr>
<td>Others</td>
<td>5</td>
</tr>
<tr>
<td>Total vascular isolation</td>
<td>7/21 (33)</td>
</tr>
<tr>
<td>Abscess/bile leak</td>
<td>4</td>
</tr>
<tr>
<td>Others</td>
<td>2</td>
</tr>
<tr>
<td>Death</td>
<td>1</td>
</tr>
<tr>
<td>Longmire clamping</td>
<td>20/20 (10)</td>
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<tr>
<td>Abscess/bile leak</td>
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</tr>
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<td>Others</td>
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<tr>
<td>No vascular control</td>
<td>2/15 (13)</td>
</tr>
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<td>Abscess/bile leak</td>
<td>1</td>
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<tr>
<td>Postoperative fever</td>
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**Figure 4.** Patterns of disease are noted by the overall incidence of recurrence and hepatic-specific recurrences. TVI indicates total vascular isolation; NVC, no vascular control.
utes. Bismuth et al\textsuperscript{8} and Emre et al\textsuperscript{9} limited the cross clamping of the supraceliac aorta to patients who did not tolerate test clamping after volume preloading. These studies demonstrated that excellent results could be obtained with minimized bleeding and limited hepatic ischemia or reperfusion injury. In our group, we reserved the use of TVI for complex tumors that required extensive resections. We also avoided supraceliac aortic cross clamping in all applications of this technique by aggressive volume preloading before test clamping.

The concept of selective vascular clamping was reported by Bismuth et al\textsuperscript{8} and Malassagne et al.\textsuperscript{11} With modern advances in techniques of liver surgery, nonvascular-related complications have replaced hemorrhage as the principal cause of poor outcome following hepatectomy, especially in patients with underlying liver disease. In selective vascular clamping, inflow occlusion of the appropriate branches of the hepatic pedicle is limited to the tumor-bearing lobe to be resected. This method of vascular control effectively eliminates the warm ischemia experienced by the nonaffected lobe. The use of the Longmire clamp accomplishes this same end point without necessitating hilar dissection in patients not undergoing lobar resection. The Longmire clamp, similar to selective vascular clamping, prevents ischemia or reperfusion injury in the residual, nonresected liver. The benefit of this method is the use of a large external compression device that controls all division line bleeding, simplifying the dissection and allowing pinpoint ligation of vessel or bile duct leakage.

In our review, TVI was used for more complex and larger lesions but did not incur a statistically larger blood loss or necessitate significantly more blood transfusions. There was, however, a trend toward a higher rate of both complications and tumor recurrence with this technique. This is most likely a reflection of extent of disease, since intrahepatic recurrence rates were not a function of resection technique. Although nonvascular isolation appeared to be an effective method of vascular control, with limited blood loss and complications, this method should be limited to peripheral lesions of the liver, where it is associated with obtaining an adequate resection margin and resultant low intrahepatic recurrence rates. Longmire clamping, like selective vascular clamping, allows control of the affected lobe without compromising the noninvolved hepatic lobe and provides a clean surgical field for meticulous dissection and both vascular and biliary ligation. All methods, despite their inherent ability to limit warm ischemia, resulted in equivalent margins. The Longmire group had the lowest incidence of recurrent disease but the highest incidence of noncolorectal metastases and an equivalent extent of disease compared with other groups.

Despite controversy over the best method of vascular control, this study indicates that multiple methods of vascular control can be used depending on the location of tumor, the extent of the resection required, and individual surgeon preference. In our experience, 2 methods of vascular control are now generally used. The application of the Longmire clamp simplifies surgery and provides a margin of safety in the resection of hepatic tumors located centrally or those requiring lobectomy or extended lobectomy. This method in our hands results in equivalent resection margins and decreases the incidence of postoperative complications, especially postoperative bile leaks. This may be the direct result of the ability to point ligate both vascular pedicles and biliary ducts. Intermittent Pringle maneuver combined with intraoperative hemodilution and low central venous pressure anesthesia is an alternate method of limiting blood loss and transfusion risks preferred by some surgeons in our group.

In conclusion, the liberal use of vascular occlusion during liver resection has led to increased safety of the procedure, aiding in the ability to perform segmentally based resections. Surgeon preference and individual experience must be the deciding factor in determining the most appropriate technique based on the clinical situation and intraoperative findings. Further studies may delineate that methods of selective vascular control convey a protective role over either inflow alone occlusion or TVI, especially in patients with compromised hepatic parenchyma who are at risk for postoperative hepatic insufficiency.

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REFERENCES

C. Wright Pinson, MD, Nashville, Tenn: The purpose of the operative period that we don't expect really has to do with the some of the hepatic dysfunction that we experience in the post-porta and/or the inferior vena cava. Or do we? Do you think we get away without anticoagulation when we are clamping the routinely anticoagulate when we clamp major vessels. Why do...

Pringle then applied the technique in 2 clinical cases; the technique provided perfect control of the bleeding areas of the liver and a clear field for operating.

C. Wright Pinson, MD, Nashville, Tenn: The purpose of the various hepatic vascular isolation techniques is to decrease blood loss, stabilize hemodynamics, avoid air embolism, and finally allow a more precise dissection in a bloodless field. Whether any of these methods is superior for reaching those goals in this report is not clear. With TVI, the higher operative mortality, blood loss, transfusion, and complications are conformed by the larger tumors in more central locations requiring more extensive resection. This is a major study design fault. But, this is true for almost all of the papers on this topic. However, Belghiti in 1996 reported a randomized prospective trial in 52 patients undergoing a major lobar resection with intermittent Pringle vs TVI. They reported higher morbidity with TVI and thus recommended TVI only for cases with tumor involving the cava.

In our reported experience of 134 resections for colorectal metastasis at Vanderbilt, we used TVI in 19% and Pringle maneuver in 27%. We also experienced higher blood loss and operative mortality with TVI. But, just as with the current report, this was confounded by the more complex resections. Nevertheless, we concluded that TVI must be used cautiously with TVI and thus recommended TVI only for cases with tumor involving the cava.

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The Pringle maneuver was initially developed and used by J. Hogarth Pringle, FRCS, from the Glasgow Royal Infirmary. Following a series of unsuccessful operations on the liver, Pringle turned to the laboratory in search of a solution to control hepatic bleeding. He used rabbits as had his predecessor Ponfick. Four of these animals were anesthetized with chloroform, the abdomen was opened, and the portal vessels clamped with a narrow forceps. During this period, the surface of 1 lobe of the liver was freely cut into at several places but no bleeding followed, and at the termination of 1 hour this lobe was removed. There were no significant changes in the small bowel. In all 4 rabbits the hemorrhage was completely controlled; the animals recovered from the operation and developed no abnormal symptoms. The rabbits were killed on the third or fourth day, temporary obstruction of the portal circulation did not appear to have injured the animals, and the experiments were discontinued.

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patients will maintain their systolic blood pressure with volume resuscitation and, if not, we do not go ahead with TVI and instead consider veno-veno bypass. In terms of the Pringle maneuver, we usually clamp for a 15- to 20-minute period up to a warm ischemia time between 60 and 90 minutes and release the clamp for 5 minutes intermittently to allow perfusion. In our series that we presented today, there were no instances of veno-veno bypass, but certainly you should be ready to perform that procedure at any time that you are considering TVI.

Dr O’Connell, your question, which is probably the most germane question, is how do we select which procedure to apply to an individual patient. For each individual surgeon in our group, and we work very closely with our transplant section, and the resections are really evenly split between the Section of Transplant Surgery and the Section of General Surgery, it is based on personal preference. I had never seen the Longmire clamp until I came to the University of Chicago, and when I was first handed the instrument when thinking about doing a resection, I was waiting for them to hand me handcuffs and a leather mask at the same time. But clearly in our group there are people who are very comfortable with the procedure and believe that it is the best way to proceed with resection and reduce bleeding. I believe that it is individual preference and location and extent of tumor that determines which procedure we prefer.

In terms of postoperative complications related to ischemia, it is very difficult to weed out which complications are due to ischemia. We certainly have elevations in bilirubin and liver function abnormalities, and there is obviously more evidence available when residents obtain more blood work than we need. But in fact we did not have any incidences of extended hepatic failure in our group. The length of stay, which I think is obviously the best indication of our complication rate, for the entire group was between 5 and 8 days, with a median of approximately 6 days after resection.

Dr Tyburski, how do we avoid or when do we consider using supraceliac clamping in addition to TVI? We have not done that in any of our patients. There are certainly groups who recommend that addition to the technique. Our approach is that, when we are in trouble in that situation and we cannot control bleeding, to go on to veno-veno bypass and not consider supraceliac clamping.

ARCHIVES OF INTERNAL MEDICINE

Early Switch From Intravenous to Oral Antibiotics and Early Hospital Discharge: A Prospective Observational Study of 200 Consecutive Patients With Community-Acquired Pneumonia

Julio A. Ramirez, MD; Sergio Vargas, MD; Gilbert W. Ritter, BSPharm; Michael E. Brier, PhD; Allie Wright, RN; Scott Smith, BSPharm; David Newman, BSPharm; John Burke, MSPharm; Mian Mushtaq, MD; Anna Huang, MD

Objectives: To determine the proportion of patients who can be treated with early switch to oral antibiotics and early discharge, to evaluate clinical outcome and patient satisfaction for patients treated with early switch and early discharge, and to define the factors that interfere with early discharge for some of the patients who underwent early switch to oral antibiotic therapy.

Design: Prospective study.

Participants: Two hundred consecutive hospitalized patients with community-acquired pneumonia.

Main Outcome Measures: Number of days needed to switch to oral therapy and length of hospital stay. Clinical outcome and satisfaction with care were evaluated for those patients treated with early switch and early discharge.

Results: Early switch to oral antibiotics (within the first 3 days of hospitalization) was performed in 133 patients (67%). Clinical failure was documented in 1 patient. Early switch and early discharge was performed in 88 patients (44%). The mean length of hospital stay for this group was 3.4 days. The most common reason for prolonged hospitalization after the switch to oral antibiotics was the need for diagnostic workup. More than 93% of patients were satisfied with the care they had received.

Conclusions: Using simple clinical and laboratory criteria, a significant proportion of hospitalized patients with community-acquired pneumonia (44%) can be treated with early switch and early discharge. This model did not affect patient outcome, decreased the length of hospitalization, and was associated with a high level of patient satisfaction. (1999;159:2449-2454)

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