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Endoscopic Retrograde Cholangiopancreatography - Analysis of 543 Procedures at the Kreiskrankenhaus Schongau [Schongau Hospital] 2006-2011 and Comparison with Literature

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Abstract

Background: Despite progress in non-invasive imaging methods of the bile and pancreatic duct, ERCP and endoscopic sphincterotomy are live methods and continue to provide the means for therapeutic intervention and cytological diagnostics. Because of the invasive and high-risk character of these methods, health professionals worldwide are attempting to minimize complication rates. There is a growing opinion throughout the scientific community that invasive procedures such as ERCP and EPT should only be performed at large centers with a high examination frequency and consequently practice related lower rates of complications. In Germany, this aim is currently supported by law. There is an existing trend to close down smaller hospitals – predominantly in rural areas. To a certain degree,the political agendas that would make these closures are motivated by economics. However, long travel times for patients, the lack of social support, the lack of knowledge of a patient's entire medical history and the ties of a patient to a near-by hospitals are set off against quality. The aim towards specialization is further accelerating this development. In this study, we were able to show that a small hospital with a well-trained medical staff can provide an equal or even better quality of care than major centers.

Methods: For the present study we retrospectively analyzed the complication rates of endoscopic papillotomies over a period of six years (from 2006 to 2011) in the gastroenterological department of the Kreiskrankenhaus Schongau [Schongau Hospital], part of a community hospital in Upper Bavaria. Overall 543 examinations were evaluated. Our data were then contrasted with international studies.

Results: Several studies were identified that evaluated ERCP and endoscopic papillotomies with comparable criteria and a comparable group of patients. With a success rate of 93.74%, the Schongau Hospital had significantly higher result than the studies.

The success rate is specified from 88% (n = 176), 90% (n =1242) to 91.6% (n = 2553). Additionally, with regard to moderate or severe post-interventional pancreatitis, the Schongau Hospital is well below the figures given in the literature: there is a mild pancreatitis in 44.8% (n = 262), moderate in 43.8% (n = 256) and severe in 11.4% (n = 67) of all patients. In Schongau, a moderate post-interventional pancreatitis occurred in 0.37% (n = 2) and a severe case in 0.18% (n = 1) of all patients. Our data shows outstandingly low rates of bleeding, acute post-interventional cholangitis or perforation when compared to the relevant literature.

Conclusions: Although the Schongau Hospital is relatively small (180 beds), it achieved equal or even better results in

terms of endoscopic sphincterotomy than major centers. This may be due to the experienced endoscopic staff, regular and intensive skill enhancement as well as the strict indication for endoscopic sphincterotomy. Our study shows that size does not matter as long as personal motivation and skill sets are excellent, and quality assessments should note this.

Keywords: ERCP; EPT; Choledocholithiasis; Post-interventional Pancreatitis; Precut; Biliary Obstruction; Pancreatic Duct Stenting; Complications of ERCP and EPT

Introduction

Cholecystolithiasis occurs in about 66% of the elderly population over 70 years of age [1]. More than 98% of bile duct disorders are caused by gallstones [2] . 10 to 33% of patients with gallstone related symptoms suffer from choledocholithiasis [3-6]**.** Patients with common bile duct stones suffer from a variety of symptoms such as cholestasis, pain, cholangitis or pancreatitis [7,8] . In addition to common bile duct stones, there are other causes of biliary obstruction such as tumors or trauma [9]. Via abdominal ultrasound, an acute cholecystitis and variations in the biliary tract such as bile duct expansion can be displayed [10,11]. To diagnose common bile duct stones, ultrasound must be combined with other imaging techniques [12]. In this case, intraoperative high-resolution sonography is indeed superior to intraoperative cholangiography in the diagnosis of small bile duct stones, assuming there is an experienced examiner available [13]; however, it does not provide a type of therapy.

Despite new imaging methods of the bile and pancreatic ducts, such as magnetic resonance cholangiopancreatography (MRCP), endoscopic retrograde cholangiopancreatography and endoscopic sphincterotomy are live imaging methods and continue to provide the only means for minimally invasive therapeutic interventions. These interventions include stone extraction from the bile duct and dilatation in case of stenosis of the major duodena papilla and the obtaining of biopsy material for cytological examinations. It also provides the only way to plant nasobiliary probes and stent placement into bile or pancreatic ducts.

Nevertheless, it is an invasive procedure that involves - according to the intention and realized intervention- risks of varying severity and therefore requires a strict indication.

The most common complication is the so-called post-ERCP pancreatitis [14]. An increase of serum pancreatic enzymes occurs in approximately 75% of patients. An acute pancreatitis, which is defined by new onset or worsened abdominal pain and the need for hospitalization, shows an increase in serum amylase and / or serum lipase of more than twice the initial value (determined 24 hours after endoscopy) and is observed in about 3.5% of patients [15]. Some studies show an incidence

of even up to 7% [16].

Other possible complications are post-interventional cholangitis, bleeding, and perforation [17].

Due to these facts, health professionals worldwide are attempting to minimize the risk of complications of endoscopic retrograde cholangiopancreatography. Achievements might be made by the technical improvement of endoscopes and papillotomes, the more consistent and more sophisticated monitoring of the patient during and after the examination, the improvement of anaesthesiological treatment options and generally by the increasing experience in this field of procedures.

There is a general understanding that well-trained and more experienced medical professionals are less likely to make mistakes and can provide a better standard of care. This supports an opinion within the scientific community that ERCP and EPT (Endoscopic papillotomy) should only be performed at large centers with a high examination frequency and therefore more experienced endoscopists [49,50]. In Germany, this aim is currently supported by law (enacted in July 2015). The current trend is to close smaller hospitals – predominantly in rural areas. To a certain degree,the political agendas that would make these closures are motivated by economics. However, long travel times for patients, the lack of social support, the lack of knowledge of a patient's entire medical history and the ties of a patient to a near-by hospital are set off against quality. The aim towards specialization is further accelerating this development.

Material and Methods

The objective of our study was to show whether a relatively small hospital is able to achieve equal or even better quality in terms of endoscopic sphincerotomy than major centers. We compared complication rates of the endoscopic department of the community *Kreiskrankenhaus* Schongau (180 beds) in terms of diagnosis and treatment by endoscopic- retrograde cholangiopancreatography and endoscopic papillotomy with literature.

The study was conducted by Professor Dr. med. Ursula Gresser, professor for Internal Medicine at the medical faculty of the LMU. According to the guidelines of the Ethics Committee of the Medical Faculty of the University of Munich all patients gave informed consent for the evaluation of the data. Before beginning, the clearance certificate of the Ethics Committee of the Medical Faculty of the University of Munich was assured.

For the study, the documentation of endoscopic papillotomies at the Schongau Hospital from 2006 until 2011 were retrospectively analyzed in terms of diagnostic results and complication rates. The comparison only included studies in which an endoscopic sphincterotomy was performed as part of the ERCP. The

comparison was performed in respect to standardized sheets of case reports, which were implemented by the unit for the hospital's quality assurance. Anamnestic, clinical, radiological, and laboratory chemistry data were used. Parameters and values which were not entered in the standardized sheets were appended from archived patient records to evaluate as many cases as possible. All missing parameters were appended from the archived records so that no examination had to be excluded from the comparison.

Unfortunately, the sheets used may not be printed due to copyright reasons. Copyright in the documentation forms is in the hands of the German Register of Papillotomy.

The personal data for this retrospective analysis, were made anonymous.

Complications were defined as follows: A mild post-interventional pancreatitis is defined by new onset or worsened abdominal pain, prolonged hospitalization or the monocausal requirement of hospitalization and an increase in serum amylase and / or serum lipase to more than twice the initial value (determined 24 hours after endoscopy). A moderate post-interventional pancreatitis is defined as a rise in amylase and / or lipase by more than twice the initial value and additionally the need of pain therapy for at least four, but not more than for ten days. A severe post-interventional pancreatitis is defined as a rise in amylase and /or lipase more by than twice the initial value and the need for pain therapy for more than ten days; in addition, morphological signs of a necrotizing pancreatitis may occur and the necessity for intervention in the form of drainage or surgery.

A post-interventional cholangitis was defined by fever (more than 38.5°C), and rising cholestastis parameters confirmed by a laboratory.

A successful endoscopic papillotomy was defined by accessing the bile duct or pancreatic duct for examination and therapy during a single session.

Bleeding was defined as bleeding that occurs during an examination that requires treatment; furthermore, bleeding was divided into non-severe, severe and bleeding requiring a subsequent transfusion.

A literature search was conducted in pubmed.gov, at the university library and in well-known professional journals.

Results and Discussion

Patient Population

The comparison group was similar to others in the existing literature [14,15,17-20]. Thus neither younger nor healthier patients were examined and treated. Furthermore, no patients had to be excluded from the study on hand because missing parameters could be appended from the archived patient records.

Success of Endoscopic Sphincterotomy

During the evaluation period, a total of 543 endoscopic papillotomies were performed. 93.74% (n = 509) of these interventions were successful the first time; only 6.26% (n = 34) of the examinations required a follow-up papillotomy in a second session. This may be due to the very experienced endoscopists working in Schongau. In comparison, the success rate in existing studies, was specified from 85% (n= 50) [21], 88% (n = 176) [18] – whereupon Lubrich`s study refers to no more than two successful sessions- , 90% (n = 1242) [17] to 91.6% (n = 2553) [19].

Bleeding Complications

Another major complication of endoscopic sphincterotomy is bleeding [19]. The frequency of severe bleeding requiring a subsequent transfusion is reported in the literature from 0.2% (n=5) [19], 0,3% (n= 4) [20] , 0.4% (n = 5) [17] , 1.1% (n= 21) [22], 1.45% (n=34) [23] to 2% (n = 2) [18]. At the Schongau Hospital, a hemorrhage requiring transfusion occurred in only one patient in 2010, which corresponds to a complication rate of 0.18%. Thus, the amount of bleeding in Schongau is significantly lower than the general number of complications in the existing literature [17-20,22]. Non – transfusion requiring bleeding occurred at Schongau in 5.71% (n = 31) of the cases. These all ended spontaneously or were able to be stopped endoscopically within the same session. A new endoscopy for hemostasis was only necessary for three patients (0.55%), however, all three endoscopies were successful. The literature states the content of non - transfusion requiring bleeding from 1.34% (n=226) [15], 3.5% (n=23) [24] to 3.8% (n=8) [18].

One possible reason may be that in the Schongau Hospital the definition of bleeding was very broad and also comprised minimal incidents, spontaneous bleeding as well as papillotomy associated bleedings were documented. Szary and Al-Kawas even describe immediate hemorrhage during papillotomy in up to 30% of patients [25]. Cotton et al. also describe the problem of a lack of a precise definition of how strong the bleeding must be to be considered a complication [26].

It is also worth mentioning that Andriulli et al. described a bleeding - related mortality rate of 3.54% (n = 8) [15]. At the Schongau Hospital, this rate is 0% (n = 0). This may be due to the attentive follow-up care practiced in Schongau.

Perforation

Another serious complication is perforation [17]. During the observed period, one perforation occurred, which was techni-

cally secured by an abdomen X-ray. This perforation was not caused by the endoscopic sphincterotomy, whereby the rate of perforation is 0% (n = 0). For the complication of perforation, frequencies of 0.5% (n= 2) [27], 0.6% (n = 101) [28], 0.8% (n= 15) [22] , 0.9% (n= 11) [20], 1.5% (n = 3) [18] to 1.8% (n= 12) [24] can be found in the literature, with a high mortality rate of up to 9.9% (n = 10) [28]. The good results Schongau achieves in terms of perforation may be produced by the strict and careful indication for endoscopic papillotomy and the experience of the physicians performing the endoscopies; it is not unusual that two experienced examiners perform the intervention together in difficult patients.

Post-interventional pancreatitis

The most common and most feared complication of ERCP is post-interventional pancreatitis [14]. Its incidence is 0.2% [19], 3.47% [28], 3.5% (n= 23) [24], 4.0% (n= 579) [29] and 4.0% [27] , sometimes even up to 4.76% [18] in the literature. During the study by Masci et al.,edematous pancreatitis occurred in 1.68% (n = 41) and necrotizing in 0.12% (n = 3) of all patients [30]. In the study by Freeman et al., pancreatitis occurred in 5.4% (n = 127) of cases [23]. In the study by Cheon et al., mild pancreatitis occurred in 2.9% (n = 422), a moderate in 0.8% (n = 108) and a severe in 0.3% (n = 49) of all patients [29]. In the Schongau Hospital, there was a total of 4.23% (n = 23) for the occurrence of post-interventional pancreatitis, which corresponds to literature [18,19,28]. However, it must be stated that mild pancreatitis occurred in 86.96% (n = 20) of all cases, moderate in 8.69% (n = 2) and severe pancreatitis in only 4.35% (n = 1) of the cases; none of them ended fatally. In this case, the Schongau Hospital is significantly lower in regard to moderate or severe pancreatitis than the values reported in the literature: there is a mild pancreatitis in 44.8% (n = 262), moderate in 43.8% (n = 256) and severe even in 11.4% (n = 67) [28] of the cases indicated. In Schongau, a moderate pancreatitis occurred in 0.37% (n = 2) and severe one in 0.18% (n = 1) of all examined patients. The good results may be due to the strict patient selection. Before the indication for ERCP or endoscopic papillotomy is set, patients are examined by means of non-invasive techniques such as abdominal ultrasonography; ERCP and endoscopic papillotomy are only performed if a benefit for the patient is expected.

Precut

Interestingly, Testoni et al. dedicate themselves in their study the increase in risk for a post-interventional pancreatitis by a precut [14]. It can be seen that for patients for whom a precut is carried out, there is a significantly (P <0.001) higher risk (7.6%) for post interventional pancreatitis than for patients for whom no precut is carried out (3.3%) [14]. In Barthet et al., 8% of all patients who were precut, developed pancreatitis [24]. In Freeman et al., 24.3% of patients, for whom a precut was performed, suffered from complications [23]. Also, in Boender

et al., a significantly higher rate of complications appeared in patients to whom the precut has been applied:

These complications were bleeding 10% (n = 5) versus 5.2% (n = 10), in terms of post-interventional pancreatitis 6% (n = 3) compared to 0.5% (n = 1), wherein perforation 8% (n = 4) versus 0% and in terms of post-interventional cholangitis 10% (n = 5) compared to 3.1% (n = 6) [31].

In his work, Huibregste comes to the conclusion that a difficult cannulation and the implementation of precuts includes the largest technology-related risk factors for complications [32].

In the Schongau Hospital, a precut was performed in 22.28% (n = 121) of the cases. 5.78% (n = 7) of the patients who received a precut suffered from a mild, 0.83% (n = 1) from a moderate and 0.83% (n = 1) from a severe post-interventional pancreatitis. In comparison to the patients for whom no precut was performed, only 2.6% (n = 11) suffered from a mild post-interventional pancreatitis and 1.65% (n = 2) from a moderate case. A severe pancreatitis occurred only after precut. The good results may be due to the awareness of the risks of precutting in Schongau; a precut is performed only if it is unavoidable.

Acute post-interventional cholangitis

The acute post-interventional cholangitis also represents a dreaded complication of ERCP [17]. The mortality rate is indicated up to 16% [33]. In the *Kreiskrankenhaus* Schongau, it occurred in 0.37% (n = 2), both times in 2008. The literature values are 0.08% (n = 2) [19], 0.5% (n = 1) [18], 0.9% [27], 1.0% (n = 24) [23], 1.1% (n = 13) [20], and 2% (n = 31) [17]. In this case, the hospital ranks better than average [17-20,23]. The results may perhaps be improved by checking the indication for prophylactic antibiosis more carefully.

Pancreatic duct filling

Testoni et al. note that a filling of the pancreatic duct by contrast agents increases the risk for post-interventional pancreatitis [14]. They even set up the following thesis: "Hydrostatic injury from pancreatic duct overfilling is very likely the main trigger of the pancreatic reaction"[14]. In the Schongau Hospital, no filling of the pancreatic duct was carried out for 43.65% (n= 237) of patients. In this group, 97.89% (n= 232) did not suffer any post-interventional pancreatitis, while 2.11% (n = 5) suffered from a mild post-interventional pancreatitis. A moderate or severe pancreatitis did not occur in this group. Filling was provided to 56.35% (n = 306) of the patients, whereas in 36.09% (n = 196) of those the pancreatic duct was filled once. 3.57% (n = 7) of these developed a mild, 0.51% (n = 1) a moderate and 0.51% (n = 1) a severe post-interventional pancreatitis. In 13.99% (n = 76) of all patients, the pancreatic duct was filled twice. 3.95% (n = 3) of these patients contracted a mild and 1.32% (n = 1) a moderate pancreatitis. The pancreatic duct was filled three times in 4.79% (n=26)of all patients;

11.54% (n=3) of these patients contracted a mild pancreatitis. The pancreatic duct was filled four times in 0.74% (n=3); none of these patients suffered from post-interventional pancreatitis. Five times or even more often pancreatic duct filling was carried out at 0.92% (n= 5). In this group, 20% (n= 1) contracted post-interventional pancreatitis. The risk of developing a post-interventional pancreatitis appears to rise with the number of injections to the pancreatic duct. Since the results of our study became available, the necessity of pancreatic duct filling in Schongau is reviewed even more attentively.

Mortality

In the Schongau Hospital, no patient died during the endoscopic sphincterotomy or from consequences and complications therefrom; the mortality rate is 0% (n = 0). In the existing literature, mortality rates from 0.1% (n=3) [19], 0.19% (n=7) [14], 0.33% (n=55) [28], 0.4% (n= 11) [22], 1.0% [20] to 1.7% [27] are stated**.** Thus, the Schongau Hospital is better than average [14,19,28]. The good result may be attributable to the attentive monitoring of patients during and after examination, as well as by the skilled endoscopists and anaesthesiologists.

Prophylaxis of post interventional pancreatitis and post-interventional cholangitis

Antibiosis

Subhani et al. recommend antibiotic prophylaxis during ERCP in certain cases [32]. For patients who have a high risk of endocarditis, for example, who have an artificial heart valve, antibiotic treatment is recommended even before the investigation [33]. For patients with biliary obstruction, an antibiotic therapy is recommended until reaching complete biliary drainage [33,34]. In the study, however, cholangitis is only prevented, pancreatitis is not treated [33]. The author expects a prevention of cholangitis in 80% of all cases [33]. In the Schongau Hospital, no antibiotics for the prevention of cholangitis were administered - except routine antibiotic prophylaxis for patients with a high risk for endocarditis. Nevertheless, in Schongau only 0.37% (n = 2) of patients contracted acute post-interventional cholangitis. This may be due to the skilled carrying out of the ERCP and EPT; anyway, indication for prophylactical antibiosis is now screened more carefully after consciousness of literature.

Stenting

The lack of complete drainage of the biliary tract is the most common cause of post-interventional cholangitis or sepsis [33,34]. In principle, Devière performs a therapeutic ERCP (endoscopic sphincterotomy or stent insertion) in the case of the emerging of a stenosis or bile duct stones during a diagnostic ERCP [34]. In this case, the rate of septicemia producing cholangitis is reduced to 0.16% [34]. How many patients suffer from a post-interventional cholangitis without subsequent sepsis is not specified [34].

In the Schongau Hospital, a stent was inserted into the bile duct of all patients after stone extraction, for whom no complete biliary drainage was achieved. This may explain the low number of post-interventional cholangitis since the biliary drainage has been ensured.

Even with an obstruction that is caused by chronic pancreatitis, Devière et al. recommend stent insertion [35]. Freeman, Tanner et al, Mazaki et al. and Andriulli et al. also recommend prophylactic stenting for patients with a high risk for post-interventional pancreatitis [28,36-38]. Freeman goes as far as to say that the evidence of the benefits of a pancreatic stent for prophylaxis in high-risk patients is irrefutable [39]. Dumonceau et al. indicate in their study the blatant discrepancy between the scientific evidence that speaks for prophylactic stenting of the pancreatic duct and its routine insertion [40]. It must be considered in this context that stent insertion into the pancreatic duct is connected with subsequent changes and does not lead in an elimination of the stricture after stent removal permanently [41]. In patients with non-resectable tumors in terms of palliative therapy, non-operable patients and to the elimination of jaundice preoperative – in accordance with Devière et al. causes a pronounced jaundice and an increase in morbidity and mortality- should stenting of the pancreatic duct be considered [42]. Moreover, Cremer et al. achieve a very significant decrease in pain or even freedom from pain after stenting of the pancreatic duct in 94% (n = 71) of patients with chronic pancreatitis [41]. Patients with recurrent acute pancreatitis benefit according to Delhaye et al. from a stent placement in the pancreatic duct [43]. In the Schongau Hospital, a stent was prophylactically inserted into the pancreatic duct in 4.42% (n= 24). Of these, 10.86% (n = 2) suffered from recurrent pancreatitis and 16.29% (n = 3) from chronic pancreatitis. However, the majority of patients in whom a pancreatic stent was introduced prophylactically, namely 32.58% (n = 6), suffered from papillitis stenosans. Good therapeutic success was reached - only one patient required a second papillotomy, complications such as pancreatitis or cholangitis did not occur.

Prophylaxis with NSAIDS

Several studies deal with how the risk of post-interventional pancreatitis can be reduced with NSAIDs. In the study of Sotoudehmanesh et al., a significantly higher rate (p = 0.03) in moderate and severe pancreatitis showed up in the group which received the placebo instead of indomethacin [44]. In the study of Elmunzer et al., in which the NSAID diclofenac has been administered, patients developed 64% less mild pancreatitis and 90% less moderate and severe pancreatitis [45].

Khoshbaten et al. conclude that diclofenac applied rectally immediately after ERCP can reduce the risk for post-interventional pancreatitis [46].

Tammaro et al. see a general benefit in the indomethacin application; however, further studies are needed to optimize the dose and the time of application [47].

Thaker et al. recommend the unique rectal application of indomethacin in high risk - patients [48].

In this context, it should be noted that in the Kreiskrankenhaus Schongau rectal application of indomethacin in high-risk patients was also begun. However, this was done only after the completion of data collection, a comparison is therefore not possible from the data available.

Evaluation and Conclusions

The data for the endoscopy unit of the Kreiskrankenhaus Schongau, regarding the success rate of endoscopic sphincterotomy and their complication rates, shows equal, sometimes even better results than in the existing literature. This could be because the examinations were only carried out by two experienced endoscopists. Thus, every examiner regularly carried out many endoscopic papillotomies. Williams et al. and Kowalski et al. found in their studies that an investigation volume that is too low may result in a loss of quality within the EPT [49,50].

Also Petrini believes that although less complicated maneuvers such as sphincterotomy, stone extraction, and stenting – if a competent radiological and surgical background is present – these procedures can be performed by well-trained endoscopists, but more complicated cases such as the biliary and pancreatic manometry, drainage of pancreatic cysts, and patients with Billroth II gastrectomy should be performed by ERCP specialists [51] . Muller agrees with him [52].

Baron et al. require that in more than 85% of all cases a competent endoscopist will be able to extract stones from the biliary tract by sphincterotomy and balloon or basket extraction [53].

Kapral et al. also state that a number of more than 50 ERCPs per year achieve higher success rates and lower complication rates [54].

Another aspect which led to the low rates of complication is that the Kreiskrankenhaus Schongau practiced strict indication for endoscopic sphincterotomy with use of endoscopic ultrasonography and magnetic resonance imaging for patient selection.

Woods et al. indicate that the most effective means of prevention of post-interventional pancreatitis is prior proper patient selection and identification of risk factors [55].

Silviera et al. conclude that the experience of the examiner, the avoiding of unnecessary investigations, the adequate preparation of the patient as well as the extremely precise attention to detail help to minimize the ERCP-related complications [56].

Kahaleh et al. state that the only effective way to avoid postinterventional pancreatitis is avoiding ERCP with marginal indications, particularly in patients at high risk for complications [57].

ERCP and EPT remain risky interventional procedures that require a strict indication, good patient preparation, and an experienced examiner to keep complication rates as low as possible. To reduce the rate of complication such as the avoidance of a precut and the filling of the pancreatic duct can help.

With this study we could contribute to the ongoing discussion, whether state of the art quality care can only be provided by large centers. Our study shows that if there is a skilled, well-trained endoscopist, the standards of major centers can be reached or even outbalanced – in addition to the advantages of patients' home-near supply. This can be improved by quality assurance institutes such as the German Papillotomy Register. Further prospective, randomized studies would be reasonable to determine, whether qualified patient care and treatment is only feasible in major centers – or if smaller hospitals with skilled staff can offer just as well qualified patient-centered care, moreover combined with advantages of home-near supply and as the case there may be even economic benefits.

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