Prevalence of Fat Embolism After Total Knee Arthroplasty Performed with or without Computer Navigation

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Background: Total knee arthroplasty performed with computer-assisted navigation without breaching of the femoral medullary canal may decrease the prevalence of fat and/or bone-marrow-cell embolization. We performed this study to determine whether the use of navigation for primary total knee arthroplasty resulted in a different prevalence of fat and/or bone-marrow-cell embolization.

Methods: We enrolled 160 patients (210 knees) who were scheduled to undergo primary total knee arthroplasty with navigation and 160 patients (210 knees) who were scheduled to undergo primary total knee arthroplasty without navigation. Arterial and right atrial blood samples were obtained before insertion of a femoral alignment rod or cutting of the distal part of the femur (baseline); at one, three, five, and ten minutes after insertion of an alignment rod or cutting of the distal part of the femur; before insertion of a tibial component broach (baseline); at one, three, five, and ten minutes after insertion of a tibial component broach; and at twenty-four and forty-eight hours after the operation. We determined the presence of fat emboli and bone-marrow-cell emboli in histologic preparations of the blood samples.

Results: The prevalence of fat embolization was 49% (102 of 210 knees) in the total knee arthroplasty group managed with navigation and 52% (109 of 210 knees) in the total knee arthroplasty group managed without navigation ($p = 0.2674$). The prevalence of bone-marrow-cell embolization was 17% (thirty-six of 210 knees) in the group managed with navigation and 15% (thirty-one of 210 knees) in the group managed without navigation ($p = 0.2591$)

Conclusions: The prevalence of fat and/or bone-marrow-cell embolization was not significantly different between the patients who underwent total knee arthroplasty with navigation and those who underwent it without navigation.

Level of Evidence: Therapeutic Level II. See Instructions to Authors for a complete description of levels of evidence.

Perioperative hemodynamic changes and postoperative pulmonary and neurologic complications secondary to fat and/or bone-marrow-cell embolization events have been reported after total knee arthroplasty[1-4]. We and others believe that these fat and/or bone-marrow-cell embolization events occur secondary to elevated intramedullary pressures generated by insertion of intramedullary alignment rods[1,5]. Computer-assisted navigation was developed to allow accurate intraoperative positioning of the components without breaching the medullary cavities[6]. This may decrease the prevalence of fat and/or bone-marrow-cell embolization.

We wished to determine whether the prevalence of fat and/or bone-marrow-cell embolization would be lower in patients undergoing total knee arthroplasty with computer-assisted navigation than it would be in patients undergoing total knee arthroplasty with a conventional method of insertion of intramedullary alignment rods. We also wanted to determine whether the prevalence of fat and/or bone-marrow-cell embolization was correlated with gender, age, body mass index, diagnosis, simultaneous bilateral or unilateral total knee arthroplasty, preoperative arterial oxygen tension, hemoglobin level, platelet count, fibrinogen level, triglyceride level, cho-

Disclosure: The authors did not receive any outside funding or grants in support of their research for or preparation of this work. Neither they nor a member of their immediate families received payments or other benefits or a commitment or agreement to provide such benefits from a commercial entity. No commercial entity paid or directed, or agreed to pay or direct, any benefits to any research fund, foundation, division, center, clinical practice, or other charitable or nonprofit organization with which the authors, or a member of their immediate families, are affiliated or associated.

TABLE I Demographic Data on All Patients

Parameters	Bilateral Arthroplasty	Unilateral Arthroplasty	Total
No. of patients	160	100	260
Male/female *(no. of patients)*	18/142	13/87	31/229
Age* *(yr)*	70.5 (58-84)	65.6 (56-76)	—
Diagnosis *(no. of patients)*			
Osteoarthritis	156 (98%)	98 (98%)	254 (98%)
Osteonecrosis	2 (1%)	2 (2%)	4 (2%)
Rheumatoid arthritis	2 (1%)	—	2 (1%)
Height* *(cm)*	152.5 (140-171)	151.4 (143-168)	
Body mass index* *(kg/m²)*	27.4 (22-34)	26.5 (21-31)	
Duration of operation* *(min)*	87.5 (55-170)	68 (55-81)	
Tourniquet time* *(min)*	56.7 (34-109)	51.8 (33-60)	
ASA (American Society of Anesthesiologists) class *(no. of patients)*			
I	32 (20%)	20 (20%)	
II	99 (62%)	70 (70%)	
III	29 (18%)	10 (10%)	

*The values are given as the mean with the range in parentheses.

lesterol level, blood cortisol level, antithrombin-III level, and a diagnosis of diabetes mellitus.

Materials and Methods

We prospectively enrolled 285 consecutive patients who were scheduled to undergo primary total knee arthroplasty into a randomized controlled study that had been approved by our institutional review board. We excluded twenty-five patients because they refused to participate in the study or because of inadequate preparation of histologic slides. The remaining 260 patients (420 knees), all of whom provided informed consent for participation, were included in the study (Table I). This study group included three subgroups: (1) sixty patients with bilateral total knee arthroplasty who had one navigated and one conventional total knee arthroplasty; (2) 100 patients with bilateral total knee arthroplasty who were divided into two groups, one consisting of fifty patients treated with bilateral navigated total knee arthroplasty and the other consisting of fifty patients treated with bilateral conventional total knee arthroplasty; and (3) 100 patients with unilateral total knee arthroplasty who were divided into two groups, one consisting of fifty patients treated with a navigated total knee arthroplasty and one consisting of fifty patients treated with a conventional total knee arthroplasty (Table II). In both the bilateral and the unilateral total knee arthroplasty groups, randomization between the use of a navigation system and the use of a conventional technique was determined from a sequential pool based on a table of randomized numbers.

In the sixty patients with one navigated and one conventional total knee arthroplasty, the navigated total knee arthroplasty was performed first. In the 100 patients in whom the two total knee arthroplasties were performed with the same (conventional or navigated) technique, the techniques were assigned alternately to each patient—i.e., if one patient underwent bilateral total knee arthroplasty with use of navigation support, the next patient underwent conventional bilateral total knee arthroplasty. At the time of the index operation, the mean age of the fifty patients who underwent navigated bilateral total knee arthroplasty was 71.1 years and the mean age of the fifty patients who had conventional bilateral total knee arthroplasty was 72.6 years. The age difference between the two groups was not significant ($p = 0.533$). The mean body mass index of the fifty patients who had navigated bilateral total knee arthroplasty was 27.0 kg/m^2, and the mean body mass index of the fifty patients who had conventional bilateral total knee arthroplasty was 27.7 kg/m^2. This difference was also not significant ($p = 0.598$).

In the group of 100 patients with unilateral total knee arthroplasty, navigation and conventional procedures were assigned alternately to each patient. The mean age of the fifty patients who had navigated unilateral total knee arthroplasty was 64.5 years, and the mean age of the fifty patients who had conventional unilateral total knee arthroplasty was 66.6 years. The age difference between the two groups was not significant ($p = 0.523$). The mean body mass index of the fifty patients who had navigated unilateral total knee arthroplasty was 26.4 kg/m^2, and the mean body mass index of the fifty patients who had unilateral conventional total knee arthroplasty was 26.6 kg/m^2. This difference was not significant ($p = 0.902$).

TABLE II Demographic Data According to the Laterality of the Total Knee Arthroplasty and Whether It Was Done with or without Navigation

Parameters	Bilateral Arthroplasty: One Knee Navigated and One Knee Non-Navigated in Same Patient	Bilateral Arthroplasty: Both Knees Navigated or Non-Navigated in Same Patient: Navigated	Bilateral Arthroplasty: Both Knees Navigated or Non-Navigated in Same Patient: Non-Navigated	Unilateral Arthroplasty: Navigated	Unilateral Arthroplasty: Non-Navigated
No. of patients	60 (60 knees) navigated, 60 (60 knees) non-navigated	50 (100 knees)	50 (100 knees)	50 (50 knees)	50 (50 knees)
Male/female *(no. of patients)*	7/53	6/44	5/45	7/43	6/44
Age* *(yr)*	67.9 (58-81)	71.1 (58-78)	72.6 (61-84)	64.5 (61-69)	66.6 (56-76)
Diagnosis *(no. of patients)*					
Osteoarthritis	59 (98%)	49 (98%)	48 (96%)	48 (96%)	50 (100%)
Osteonecrosis	1 (2%)	1 (2%)	—	2 (4%)	—
Rheumatoid arthritis	—	—	2 (4%)	—	—
Height* *(cm)*	152 (143-161)	150.9 (141-161)	154.5 (140-171)	152.1 (147-158)	150.7 (143-168)
Weight* *(kg)*	60.6 (50-71)	61.9 (37-85)	62.5 (41-73)	61.95 (46-74)	66.6 (51-113)
Body mass index* *(kg/m²)*	27.2 (20-36)	27 (22-34)	27.7 (23-33)	26.4 (22-31)	26.6 (21-31)
Duration of operation* *(min)*	83.2 (70-110) for navigated, 64.2 (55-90) for non-navigated	98.0 (75-110), 98.7 (80-112)	87.3 (60-106), 86.7 (60-105)	75 (65-81)	61 (55-72)
Tourniquet time* *(min)*	63.5 (53-78) for navigated, 40.3 (34-67) for non-navigated	61.1 (50-70), 62.2 (51-80)	50.3 (40-85), 50.1 (38-86)	57.7 (54-60)	45.8 (33-55)
ASA (American Society of Anesthesiologists) class *(no. of patients)*					
I	11 (18%)	11 (22%)	10 (20%)	8 (16%)	12 (24%)
II	38 (63%)	29 (58%)	32 (64%)	36 (72%)	34 (68%)
III	11 (18%)	10 (20%)	8 (16%)	6 (12%)	4 (8%)

*The values are given as the mean, with the range in parentheses.

Before the surgery, all patients had a routine preoperative medical evaluation including a urinalysis, electrocardiogram, echocardiogram, chest radiograph, and pulmonary function tests. All patients had preoperative and postoperative laboratory tests including measurements of the hemoglobin level, platelet count, cholesterol level, cortisol level, fibrinogen level, and antithrombin-III level.

An epidural normotensive anesthetic was administered to all patients with an indwelling catheter. The catheter was maintained in place for forty-eight hours postoperatively for pain control.

Before the induction of anesthesia, a 20-gauge cannula was inserted into the radial artery to monitor the blood pressure and to obtain blood samples. In addition, a catheter was placed in the right atrium through an antecubital vein to monitor the right atrial pressure and to obtain blood samples. Intravascular pressures measured with transducers, together with cardiac function, were monitored continuously on a pen recorder (Hewlett-Packard, Andover, Massachusetts). All pressures were referenced to the level of the right atrium and were expressed in millimeters of mercury (mm Hg). In addition, the percentage of oxygen saturation was monitored with a pulse oximeter (Nellcor, Hayward, California), and end-tidal carbon dioxide tension was monitored with a carbon dioxide monitor (model CD 223; Datex, Carlsbad, California); these variables, together with esophageal temperature and breath sounds, were monitored continuously during the operation and for forty-eight hours postoperatively.

The procedures were performed in a standardized manner by one surgeon (Y.-H.K.) at one institution. A bloodless field was obtained by the use of a pneumatic tourniquet at a pressure of 350 mm Hg after exsanguination with an Esmarch bandage. All patients had a unilateral or bilateral primary total knee arthroplasty with use of a cemented NexGen posterior cruciate-retaining high-flex prosthesis (Zimmer, Warsaw, Indiana) with a cemented patellar button.

When the intramedullary guides were used, all attempts were made to reduce fat and/or bone-marrow-cell embolization[3]. We overdrilled the medullary entry holes to exceed the diameter of the alignment rod to allow bone marrow contents to bypass the rod and to decrease intramedullary pressure[7]. Copious irrigation of the medullary canal was performed with pulsatile lavage. The rods, which were fluted to assist the egress of bone marrow elements, were introduced slowly to further reduce the intramedullary pressure and the likelihood of pulmonary shunting[8].

In both groups, arterial and right atrial blood samples were obtained before cutting of the distal part of the femur or before insertion of the femoral alignment rod (baseline) and at one, three, five, and ten minutes after cutting of the distal part of the femur or after insertion of the femoral alignment rod. Arterial and right atrial blood samples were also obtained before insertion (baseline) and at one, three, five, and ten minutes after insertion of the tibial component broach. Blood samples were obtained twenty-four and forty-eight hours postoperatively as well. The arterial blood pressure, heart rate, right atrial pressure, arterial oxygen tension, and carbon dioxide tension were monitored at corresponding times.

The right atrial blood samples (5 mL) were cooled and were centrifuged at 4°C, and the superficial and buffy coat layers (about 10 μL) were removed from each tube for examination. Histologic slides of specimens from the superficial layers were prepared, and the presence of fat emboli was determined with oil-red-O stain and the presence of cellular contents of the bone marrow was determined with Wright-Giemsa stain[9]. The total numbers of fat globules and bone marrow cells were counted with use of our previously described technique[10]. The total numbers of fat globules and bone marrow cells were counted in all blood samples from each patient (twenty samples from each patient in the bilateral arthroplasty group and eleven samples from each in the unilateral arthroplasty group). The mean, range, and mode of the number of fat globules and bone marrow cells were calculated, and these values were compared between the groups treated with navigation and those treated with the conventional technique. Blood gases were analyzed with standard electrodes at 37°C, and the values were corrected to measured body temperature.

We recorded values as the mean and the standard error. Data were analyzed with a two-tailed Student t test, a two-way analysis of variance, and the Dunnett multiple range test[11]. The differences between the groups were analyzed with use of one-way analysis of variance and the Tukey procedure[11]. For the multiple results in the sixty patients with bilateral total knee arthroplasty who had one navigated and one conventional procedure, the Tukey method was used as a multiple comparison (post hoc comparison) to determine which pair of means was different without increasing the alpha error. Also, a sensitivity analysis was performed with use of Proc Genmod (SAS Institute, Cary, North Carolina). The level of significance was set at $p < 0.05$.

Results

The overall prevalences of fat and bone-marrow-cell embolization associated with the total knee arthroplasties with and without navigation support are summarized in Table III. In the group treated with one navigation and one conventional total knee arthroplasty (sixty patients), we observed fat emboli in association with twenty-seven (45%) of the sixty knees with navigation and in association with twenty-nine (48%) of the sixty knees without navigation. This difference was not significant ($p = 0.451$). Also, a sensitivity analysis demonstrated no difference between the two groups (Z score = 0.38, $p = 0.7053$). In the group treated with navigation in both knees (fifty patients), we observed fat emboli in association with fifty-four (54%) of the 100 knees; in the group in which navigation was not used on either side (fifty patients), fat emboli were observed in association with fifty-seven (57%) of the 100 knees. This difference was not significant ($p = 0.1831$). In the group treated with unilateral total knee arthroplasty, fat emboli were observed in twenty-one (42%) of the fifty patients who received navigation and in twenty-three (46%) of the fifty patients who received no navigation. This difference was not significant ($p = 0.1681$).

TABLE III Overall Prevalence of Systemic Fat and Bone-Marrow-Cell Embolization Associated with Total Knee Arthroplasties with or without Navigation Support

Emboli	Navigated Total Knee Arthroplasty (N = 210) *(No. of Knees)*	Non-Navigated Total Knee Arthroplasty (N = 210) *(No. of Knees)*	P Value
≥1 fat globule	102 (49%)	109 (52%)	0.2674
≥1 bone-marrow-cell	36 (17%)	31 (15%)	0.2591

There was no difference in the overall number of fat emboli between the groups treated with navigation and those treated without it (mean, 15.3 compared with eighteen fat emboli per high-power field) (see Appendix). In both groups, the prevalence of fat embolization at one, three, five, and ten minutes after bone preparation of the distal part of the femur or after insertion of the femoral alignment rod was increased compared with the prevalence at baseline ($p = 0.042$). In both groups, the prevalence of fat embolization at twenty-four and forty-eight hours after the operation was higher than the prevalence at baseline.

In the group treated with bilateral total knee arthroplasty, we observed bone-marrow-cell emboli in association with eight (13%) of the sixty knees treated with navigation and in association with six (10%) of the sixty knees treated without navigation. This difference was not significant ($p = 0.4781$). Also, a sensitivity analysis demonstrated no difference between the two groups (Z score = 1.0, $p = 0.3154$). We observed bone-marrow-cell emboli in association with twenty-one of the 100 knees in the group that underwent bilateral total knee arthroplasty with navigation and in association with nineteen of the 100 knees in the group that underwent bilateral total knee arthroplasty without navigation. This difference was not significant ($p = 0.512$). Bone-marrow-cell emboli were found in seven of the fifty patients who underwent unilateral total knee arthroplasty with navigation and in six of the fifty patients who underwent unilateral total knee arthroplasty without navigation. This difference was not significant (p = 0.192). The mean number of bone-marrow-cell emboli was similar in both groups (see Appendix). In both groups, the prevalence of bone-marrow-cell embolization at one, three, five, and ten minutes after insertion of the femoral alignment rod or cutting of the distal part of the femur was increased compared with the prevalence at baseline (p = 0.041), and the prevalence of bone-marrow-cell embolization at twenty-four and forty-eight hours after the operation was higher than the prevalence at baseline.

In the group treated with bilateral total knee arthroplasty, we observed fat emboli in association with 167 knees (52%) and bone-marrow-cell emboli in association with fifty-four knees (17%). In the group treated with unilateral total knee arthroplasty, we observed fat emboli in association with forty-four knees (44%) and bone-marrow-cell emboli in thirteen knees (13%). There was no significant difference between the group treated with bilateral arthroplasty and the group treated with unilateral arthroplasty with regard to the prevalence of fat emboli (p = 0.479), the prevalence of bone-marrow-cell emboli (p = 0.891), or the overall number of fat emboli (mean, eighteen compared with fourteen) per high-power field (p = 0.672).

There was no significant difference in the intraoperative and postoperative hemodynamic values (arterial partial oxygen pressure, arterial carbon dioxide tension, saturation [percent], mean arterial pressure, mean right atrial pressure, and heart rate) between the patients treated with and those treated without navigation. In addition, there was no significant difference in the intraoperative or postoperative hemodynamic values between the group treated with unilateral total knee arthroplasty and the group treated with bilateral total knee arthroplasty ($p > 0.05$) (see Appendix).

The patients with evidence of bone-marrow-cell embolization had a lower mean arterial oxygen tension (65.6 ± 16.8 mm Hg compared with 81.3 ± 18.9 mm Hg, p = 0.025) and arterial oxygen saturation (86% ± 9.8% compared with 93.8% ± 8.7%, p = 0.026) than did the patients without bone-marrow-cell embolization one day postoperatively.

There was a higher prevalence of fat embolism (60% compared with 41%, p = 0.038) in patients with higher triglyceride levels (>180 mg/dL [>2 mmol/L]) than in patients with lower triglyceride levels (<180 mg/dL). There was no apparent association between the presence of fat globules and/or bone-marrow-cell emboli and the mean preoperative hemoglobin level (p = 0.583), mean postoperative hemoglobin level (p = 0.425), mean preoperative platelet count (p = 0.213), mean postoperative platelet count (p = 0.256), mean preoperative body mass index (p = 0.625), mean preoperative cholesterol level (p = 0.579), diagnosis of diabetes mellitus (p = 0.287), gender (p = 0.468), age (p = 0.498), mean preoperative blood cortisol level (p = 0.856), mean preoperative fibrinogen level (p = 0.924), mean preoperative antithrombin-III level (p = 0.289), or preoperative diagnosis (p = 0.537).

Before cutting of the distal part of the femur in the group treated with navigation, 12% of the patients undergoing bilateral total knee arthroplasty and 8% of the patients undergoing unilateral total knee arthroplasty had one or more fat emboli in the blood samples. Before the insertion of the femoral alignment rod in the group treated without navigation, 15% of the patients undergoing bilateral total knee arthroplasty and 10% of the patients undergoing unilateral total knee arthroplasty had one or more fat emboli present in the blood samples. Although there were no detectable bone-marrow-cell emboli before insertion of the femoral alignment rod in the group treated without navigation, 24% of the patients treated with navigation had one or more bone-marrow-cell emboli before cutting of the distal part of the femur.

Of the sixty-seven patients who had one or more bone-marrow-cell emboli, seven (three treated with bilateral total knee arthroplasty with computer-assisted navigation and four treated with bilateral total knee arthroplasty without computer-assisted navigation) had diffuse encephalopathy with confusion and agitation for approximately twenty-four hours. Serial chest radiographs of these patients showed no evidence of pulmonary infiltration. None of these patients had fat embolism syndrome, and none died.

Discussion

We explored the question of whether the prevalence of fat and/or bone-marrow-cell embolization would be lower in patients undergoing total knee arthroplasty with computer-assisted navigation than in patients undergoing total knee arthroplasty with the conventional method involving use of intramedullary alignment rods. We found that the prevalence of fat and/or bone-marrow-cell embolization was not significantly different between these two groups.

In contrast to our data, Kalairajah et al. demonstrated a highly significant (p = 0.0003) reduction in the number of cranial fat emboli, as detected with automated transcranial Doppler ultrasonography, in a group treated with computer-assisted total knee arthroplasty compared with a group treated with non-computer-assisted total knee arthroplasty[12]. Those authors, however, were not able to differentiate the fat and/or bone-marrow-cell emboli from other debris such as air, platelets, or bone with the Doppler ultrasonographic examination.

Some studies have implicated intramedullary guides as the major factor producing fat and/or bone-marrow-cell embolism by elevating the intramedullary pressure[2,4,12]. Similar findings have been reported in patients undergoing hip arthroplasty[10,13]. In our study, the prevalence of fat and/or bone-marrow-cell embolization associated with total knee arthroplasties in which intramedullary alignment guides were used was not higher than the prevalence associated with the navigation-supported total knee arthroplasties. This finding might be attributed to the technique that we used. When we used intramedullary rods, we attempted to reduce the risk of fat and/or bone-marrow-cell embolization. We overdrilled the medullary entry holes to exceed the diameter of the femoral alignment rod to allow bone marrow contents to bypass the rod and to prevent an increase in intramedullary pressure. We performed copious irrigation of the medullary canal with pulsatile lavage. We used fluted femoral alignment rods and introduced them more slowly to assist the egress of fat and bone marrow elements in an effort to avoid an increase in the intramedullary pressure.

Why fat and bone-marrow-cell emboli were detected in the patients in whom total knee arthroplasties were performed with navigation without breaching of the femoral medullary canal is not clear. The following factors might explain this finding: the preparation of the cancellous distal part of the femur and proximal part of the tibia causes mobilization of fat and/or bone marrow cells in those areas and generates fat and bone-marrow-cell emboli; the impaction of the tibial component broach and insertion of the prosthesis cause transient elevation of the tibial medullary pressure that is sufficient to produce systemic embolization of fat and bone marrow contents; and impacting of the femoral and tibial components increases the extravascular pressure, facilitating embolization.

Fat emboli were detected in our series before the insertion of the femoral alignment rod. These emboli may have arisen from subcutaneous, capsular, and synovial fat tissues of the knee joint. The bone-marrow-cell emboli detected before the preparation of the distal femoral bone in the group treated with navigation may have been produced while two bicortical tracker pins (4 mm in diameter) were inserted into the femur and the tibia.

A limitation of this study is that we do not know whether the specimens evaluated on the histologic slides were truly representative of the overall presence of fat and/or bone-marrow-cell emboli. We think that serial sampling and repeated examination of right atrial blood samples provided adequate information about fat and bone-marrow-cell embolization. Other investigators[12,14] have emphasized that transesophageal echocardiography or transcranial Doppler ultrasonography can provide a broader sampling than can analysis of the very small volume on a microscopic slide to quantitate the magnitude of fat and/or bone-marrow-cell emboli present in the right atrium. Transesophageal echocardiography, however, is limited with regard to its ability to differentiate fat and/or bone marrow cells from other debris (such as air, platelets, or bone). An additional limitation of this study is that sampling of right atrial blood was not done at the time of tourniquet release.

In conclusion, the prevalence of fat and/or bone-marrow-cell embolization was not significantly different between patients in whom total knee arthroplasty was performed with navigation and those in whom it was performed without it. Our data suggest that fat and/or bone-marrow-cell embolization can occur during preparation of the bone of the distal part of the femur and proximal part of the tibia without breaching of the medullary canal.

Appendix

eA Tables showing the results of semiquantitative analyses of fat emboli and bone-marrow-cell emboli and the hemodynamic data are available with the electronic versions of this article, on our web site at jbjs.org (go to the article citation and click on "Supplementary Material") and on our quarterly CD-ROM (call our subscription department, at 781-449-9780, to order the CD-ROM). ■

Note: The authors acknowledge the help of Soo-Young Lee, MD, for her part in interpreting the histologic slides of fat and/or bone marrow cells.

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