

Short-term efficacy of trial medicine treatment may play a predictive value for the choice of therapy methods among brain abscess patients

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Abstract

Background: Traditionally, brain abscess with diameter beyond 2.5cm is considered to be treated with surgical methods, however in some cases medical treatment alone also got good results. Which patients with the abscess diameter beyond 2.5cm could be treated with medicine alone?

Objective: 32 brain abscess patients accepted one week of trial medicine therapy and were divided into surgical group and conservative group according the ultimate therapy method.

Methods: Some clinical factors including Glasgow Coma Scale (GCS), Karnofsky performance scores (KPS), and mini-mental state examination (MMSE), abscess sizes and edema indexes (EI) were recorded, and these factors were analyzed to observe the differences between the two groups.

Results: The surgical group had larger abscess sizes ($4.21 \pm 0.62\text{cm}$ vs $2.85 \pm 0.98\text{cm}$ $p < 0.001$), lower GCS (10.00 ± 1.04 vs 11.44 ± 1.92 $p = 0.017$), lower KPS (40.71 ± 12.69 vs 52.78 ± 20.24 $p = 0.061$), and lower MMSE scores (8.57 ± 1.40 vs 11.67 ± 2.38 $p = 0.0008$) before treatment than the conservative group. After trial therapy, the conservative group got higher extent of MMSE improvement (10.06 ± 2.67 vs 4.86 ± 0.66 $p < 0.0001$) and abscesses sizes decline ($0.7 \pm 0.40\text{cm}$ vs $0.15 \pm 0.18\text{cm}$ $p = 0.0002$) than surgical group, logistic analysis indicated consecutive variation of MMSE and change of abscess sizes during trial treatment might correlated closely to the ultimate treatment methods ($p = 0.027$; $p = 0.019$).

Conclusions: These data might provide some clues for the selection of treatment methods for brain abscess patients.

Introduction

Brain abscess (BA) is a focal pyogenic infection of the brain's parenchyma with classic symptoms of headache, fever history, and focal neurologic deficits [3, 14, 4, 21]. Traditionally, it is considered that brain abscess with diameter beyond 2.5 cm should be treated with surgical method (image-guided stereotactic aspiration or resection) [14, 24, 19, 16, 2, 9, 17, 15], Whereas the abscess with diameter less than 2.5 cm can be treated with medicine alone [24, 19]. However, even with the surgical treatment, prolonged and sufficient dose of antibiotics is the basis for the brain abscess therapy [16, 8]. In fact, in our medical center, what intrigued us was that for fear of surgery some patients with brain abscess larger than 2.5 cm in diameter had been treated with medicine alone and recovered well. How to distinguish which patients could be treated with medicine alone even with abscess beyond 2.5cm?

A group of brain abscess patients accepted a week of trial medicine treatment in our medical center and were divided into surgical group and conservative group according the ultimate therapy methods. This study aimed to observe different response to one week of trial medicine treatment and find the differences of some clinical factor variations between the two groups. By these data, we want to find out what was the determinant to judge which patients with abscess beyond 2.5 cm could be treated with medicine alone. Maybe that is useful for patients reluctant to accept surgery.

Patients And Methods

Subjects

Consecutive 32 brain abscess patients accepted treatment at our hospital's department of neurosurgery from 2015 to 2018. According the ultimate therapeutic method, these patients were divided into surgical group (14 cases) and conservative group (18 cases). General data include demographic data, predisposing factors, anatomical location, symptoms and signs, final therapeutic method, and prognosis, duration of parenteral antibiotics and hospital stays were recorded according medical records. Periodic outpatient follow-up were recorded including duration of oral antibiotics outside hospital, length of time to return to normal life (or work). Written approval for this study was obtained from the ethics committee of our hospital, all patients and their family members were informed the illness condition and treatment program and they all signed an informed consent sheet.

Inclusion criteria

1. Single or multiple brain abscess confirmed by laboratory testing and imaging examination;
2. Secondary brain abscess with the primary disease being controlled well;
3. Single or multiple brain abscess with no clinical evidence of multi-systematic infections or diseases;
4. Single or multiple postoperative or posttraumatic brain abscesses.

Exclusion criteria

1. Systemic infectious disease like AIDs and uncommon specific infection such as tuberculosis, fungi, and parasites;
2. Patients with serious conditions caused by the brain abscess had to be treated with emergency surgical treatment on admission;
3. Brain abscess associated with other serious diseases such as multisystem purulent infections, serious conditions of other organs.

Clinical Diagnosis And Assessment

Brain abscess has several clinical features: 1. the classic symptoms of fever, headache, and focal neurologic deficits ^[4]; 2. Potential causes of abscess: recent history of operation or trauma, an adjacent infection, other system or organ's infection, etc.; 3. Increased leukocyte count, C-reactive protein content, and procalcitonin content in peripheral blood ^[5]; 4. Rim-enhancement T1 magnetic resonance image, restricted diffusion signal in diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) sequences ^[22]. Brain abscess could be diagnosed according these clinical features.

GCS, KPS, and MMSE scores were recorded and evaluated every day during the first initial week of trial medical treatment besides the day on admission before treatment. According the axis of T1-enhanced

magnetic resonance image, T2-weighted imaging and FLAIR imaging, image data including edema indexes (EI) and maximal diameters of abscesses were measured before and after trial medical treatment [20]. All these data were analyzed to figure out which factors were correlated with the ultimate treatment method.

According to the medical records and follow-up data, duration of hospital stay, duration of parenteral antibiotics and oral antibiotics, length of time to return to normal life between the two groups were recorded and compared.

Treatment Procedure

Each patient accepted one week of trial medicine treatment once brain abscess were confirmed. Parenteral, broad-spectrum Vancomycin and meropenem were used as initial empirical treatment combination. Parenteral metronidazole or ornidazole was added if anaerobic brain abscess which mostly originated from upper respiratory tract or chronic suppurated otitis media was suspected according to the neurological imaging and medical history.

Short-term intravenous administration of corticosteroids, mannitol was conducted in case of the increased intracranial pressure or considerably significant mass effect was indicated. When the clinical symptoms were relieved, the usage of corticosteroids and mannitol were decreased or stopped. The patients with poor response to the trial medicine treatment accepted surgical treatment.

Whether conservative group or surgical group, both groups kept parenteral antibiotics till: 1. completely remission of the clinical symptoms; 2. restricted diffusion relieved totally in DWI signal (complete low signal in DWI); 3. Obvious shrink of abscess lesion and complete remission of mass effect. And then oral antibiotics were used till two weeks after complete remission of abscess.

Flowchart of treatment process

Statistical analysis

The chi-squared test was used between two groups for qualitative comparisons. Independent-Samples T Test and Paired-Samples T Test was used for the change of clinical factors. One-way analysis of variance (ANOVA) was performed for comparisons among multiple groups, followed by a post hoc Bonferroni test. Bivariate logistic regression analysis was used to find factors related operation. Statistical significance was set at $p < 0.05$. SPSS software version 24.0 (SPSS, Chicago, IL, USA) was used for statistical analysis.

Results

1. Epidemiology And Characteristics

32 consecutive brain abscess patients included 18 males (56.25%) and 14 females (43.75%) from ages 7 to 72. In this group of patients, brain abscess mainly occurred in adults and the most common sites

affected were frontal lobe (37.50%) and temporal lobe (28.13%). Of all the cases in the surgical group, the maximal abscess diameter were beyond 2.5 cm; different from conventional conception, 11 of 18 cases in the conservative group were also beyond 2.5 cm. Most patients were cryptogenic (62.50%), and the predisposing factors of few patients included contiguous spread (6.25%), postoperative infection (12.50%), hematogenous infection (9.38%), and posttraumatic infection (9.38%) and so on (Fig. 1). Headache was the most common symptom in this group of patients (78.13%), 17 patients had fever (53.13%) and 15 cases showed meningeal irritation (46.88%), 15 patients showed focal neurological deficits (46.88%), the classical triad (fever, headache and focal neurological deficits) was relatively rare in our study (4 cases, 12.5%). Some patients showed signs of high cranial pressure such as altered state of consciousness (31.25%) and nausea,vomiting (25%). Almost every patient had various degrees of mental state alteration. No differences were found in these characteristics between the two groups according to our data (Table1) ($p \geq 0.05$).

Table 1
general characteristics of patients

characteristics	Number of patients (%)
sex	
male	18(56.25)
female	14(43.75)
age	
< 20	3(9.38)
20–40	16(50.00)
> 40	13(40.63)
location of the abscess	
frontal lobe	12(37.50)
temporal lobe	9(28.13)
parietal lobe	4(12.50)
occipital lobe	2(6.25)
basal ganglia and thalamus	5(15.63)
symptoms and signs	
headache	25(78.13)
nausea and vomiting	8(25.00)
altered state of consciousness	10(31.25)
focal neurological deficits	15(46.88)
seizures	6(18.75)
fever	17(53.13)
signs of meningeal irritation	15(46.88)
predisposing factor	
contiguous spread	2(6.25)
postoperative infection	4(12.50)
hematogenous infection	3(9.38)
posttraumatic infection	3(9.38)

characteristics	Number of patients (%)
cryptogenic infection	20(62.50)

Figure1:

Table 1 general characteristics of patients

2. Different reaction to the first week of medical treatment

With a high sensitivity and specificity, brain abscess has a high signal in diffusion-weighted imaging (DWI) [22]. According the T1-enhanced MRI and diffusion -weighted imaging (DWI) scans, brain abscess sizes declined after a week of trial medicine treatment (Fig. 2). In fact, there was a different response to the first week of trial medicine treatment between the two groups.

2.1 The change of abscess sizes during trial therapy

Being consistent with conventional view, mean maximal abscess diameters of the surgical group was larger than that of the conservative group (4.21 ± 0.62 cm vs 2.85 ± 0.98 cm $p < 0.001$) (Fig. 3a). After a week of medical treatment, brain abscess sizes of both groups got an obvious decline (the conservative group: 2.86 ± 0.98 cm vs 2.16 ± 0.70 cm $p < 0.0001$; the surgical group: 4.21 ± 0.62 cm vs 4.04 ± 0.60 cm $p = 0.0036$) (Fig. 3b and c). More obvious abscess sizes decline was detected in conservative group than that in surgical group (0.7 ± 0.40 cm vs 0.15 ± 0.18 cm $p = 0.0002$) (Fig. 3d).

2.2 The variation of EI during trial therapy

Because of the inflammatory response, brain abscess always accompany with various extent of brain edema which can worsen the patients' condition [6]. After a week of trial medical therapy the edema around brain abscess relieved in most patients (Fig. 4a, b). The edema indexes (EI) were measured according the MRI before and after a week of conservative treatment. Before treatment no obvious difference was found between the two groups (3.20 ± 0.51 vs 3.73 ± 0.97 $p = 0.057$) (Fig. 4c). Although EI got a little decrease after one week of trial medical therapy in both groups (Fig. 4d, e), however, no difference was found about the extent of EI decline between these two groups either (Fig. 4f, 0.41 ± 0.26 vs 0.51 ± 0.54 $p = 0.91$).

2.3 The variation of MMSE, GCS and KPS scores during trial therapy

MMSE scores, GCS scores and KPS scores were recorded every day. Conservative group had Higher MMSE scores than that in surgical group on admission (11.67 ± 2.38 vs 8.57 ± 1.40 $p = 0.0008$) (Fig. 5a), and after trial treatment both group got an improvement in MMSE scores (Fig. 5b and c); higher extent of MMSE scores improvement was observed in conservative group than that in surgical group, and the difference was obvious (Fig. 5d, 10.06 ± 2.67 vs 4.86 ± 0.66 $p < 0.0001$). Similarly, Conservative group had Higher GCS scores (11.44 ± 1.92 vs 10.00 ± 1.04 $p = 0.017$) (Fig. 6a) and KPS scores than in surgical group on admission, but the difference of KPS scores was not apparent (52.78 ± 20.24 vs 40.71 ± 12.69 $p = 0.061$) (Fig. 6b). After trial medicine treatment, GCS scores and KPS scores all got an obvious

improvement in both groups, and conservative group got higher extent of improvement both in GCS scores and KPS scores than in surgical group (**6c, d and Fig. 6e, f**).

2.4 The consecutive variation of MMSE and the change of abscess sizes during trial therapy correlated with the choice of final therapy method.

Consecutive changes of MMSE scores, KPS scores and GCS scores were recorded every day in one week of trial medicine treatment, although all of GCS scores, KPS scores and MMSE scores improved in both groups, the consecutive variation of MMSE scores was more obvious between the two groups (Fig. 7a, $p < 0.0001$), while no apparent difference were detected in consecutive variations of GCS scores and KPS scores between these two different groups (Fig. 7b **and c**, $p = 0.85$, $p = 0.11$). All these data showed that in these three consecutive changed clinical factors, the change of MMSE scores might be a more sensitive variable in response to the medicine therapy of brain abscess than GCS scores and KPS scores.

However, further logistic regression analysis confirmed that MMSE scores and brain abscess size might be two of the most crucial factors related surgery ($p = 0.027$; $p = 0.019$).

Outpatient follow-up lasted from 6 to 20 months (average 13.46 months). The clinical outcome was assessed at 6-months endpoint, at that time point, all patients had no abscesses identified by T1-enhanced MRI or diffusion-weighted imaging (DWI) scans (Table2). Almost all the patients had a favorable outcome (good recovery or mild disability), no dead cases existed in this group of patients, only 3 cases had drug-controlled seizures and 6 cases had mild focal neurological deficits but independent in daily lives. There was no obvious difference in the ultimate clinical outcome between these two groups.

Table 2
Differences of the whole treatment course between the two groups

	surgical group	conservative group
duration of antibiotics		
Parenteral (IV antibiotic) (days)	27.57	31.33
oral(weeks)	8.64	9.89
hospital stays (days)	29.07	33.47
length of time to return to work (months)	3.46	3.87

However, it was consistent with the conventional view, compared with the conservative group, surgical group had a shorter duration of hospital stay (29.07 ± 7.16 vs 33.47 ± 6.29 days, $p = 0.035$) (Fig. 8a), shorter duration of oral antibiotics (8.64 ± 1.74 vs 9.89 ± 1.53 weeks, $p = 0.049$) (Fig. 8c), and more quick to return to normal life (3.46 ± 0.39 vs 3.87 ± 0.55 months, $p = 0.025$) (Fig. 8d). But for the duration of parenteral antibiotics in hospital, the difference between the two groups was not obvious (27.57 ± 6.22 vs 31.33 ± 5.40 days, $p = 0.054$) (Fig. 8b).

Discussion

Conventionally, the first choice of treatment for brain abscess beyond 2.5 cm in diameter would be surgical method [16, 1]. However, there was once a patient with brain abscess diameter over 2.5 cm was reluctant to be treated with surgical method, and he had accepted conservative medical treatment in our center. To our surprise, the clinical symptoms of fever, headache, and visual field defect relieved soon after several days of medicine therapy, and abscess lesions, edema around abscess decreased obviously in MRI too. Which interested us to find out whether brain abscess beyond 2.5 cm must be treated with surgical method? Which patients with brain abscess over 2.5 cm could be treated with medicine only?

In our study, in the 18 cases of conservative treatment patients, the maximal abscess diameter of 11 was beyond 2.5 cm, and the largest one was about 4.2 cm far beyond 2.5 cm, the mean size of abscess in conservative group was 2.85 ± 0.98 cm. Our date showed that even if the abscess was bigger than 2.5 cm, medicine alone could get a good response in some cases. In fact, medicine is the basis for the treatment of brain abscess, even with the surgical therapy, patients also need a long time of medicine treatment to go. With the development of better antibiotics, more and more brain abscess patients showed good response to the medicine treatment in modern times [5, 23, 13].

The most common causative pathogens of most brain abscesses are gram positive (*streptococci* and *staphylococci*) and anaerobic bacteria [5]. In one week of trial medical treatment, we used meropenem, vancomycin and sometimes plus metronidazole as the first choice of antibiotics combination which were broad-spectrum and might cover all the likely pathogens with good ability penetrating through blood-brain barrier and into abscess cavity [10].

In fact, in this group of patients, almost everyone had responded to the first week of trial medicine therapy. Abscess sizes, GCS, KPS, mental status (MMSE), and the degree of edema around the abscess are important factors to judge the clinical status for the brain abscess [1, 7, 11, 12, 18]. After a week of trial medical treatment, almost every patient got an improvement in clinical status, but there were different changes in these factors between the two groups. Conservative group got a more obvious decline in abscess sizes (Fig. 3), more obvious improvement in MMSE scores (Fig. 5), KPS scores and GCS scores (Fig. 6) than that in surgical group. However, no obvious differences about the extent of GCS and KPS scores improvement between the two groups were observed, while MMSE scores improvement and abscess sizes decline were much more obvious in conservative group than that in surgical group after

trial medical treatment, which implied that conservative group was more sensitive to the medical therapy than the surgical group.

Compared to these factors, although both groups got a little decline in edema indexes, but the edema indexes before and after medical therapy were not obvious different between the two groups in our study. Maybe the edema around the abscess and the abscess size decreased in a certain ratio.

About all the changes of factors during one week of trial medical treatment, logistic regression analysis showed that the consecutive variation of MMSE scores and brain abscess sizes were highly correlated with the final choice of treatment methods for the brain abscess patients ($p = 0.027$; $p = 0.019$), and might be two of the most predictive crucial factors related the choice of treatment methods.

Nevertheless, surgical group had a more severe clinical condition on admission, while after surgical treatment, the surgical group recovered more quick than the conservative group (Fig. 8), which was in consistent with convention views. But for the patients who are not reluctant to accept surgical treatment, maybe the trial medicine therapy would be a good choice.

Conclusions

These data might offer some assistance to estimate the choice of individualized treatment of brain abscess, and provide some clues the decision of medicine therapy alone or surgical treatment for brain abscess patients. A little deficiency of our study was that 32 cases might be a little less; more cases will be added to find more clues for the choice of individualized treatment ways for brain abscess.

Declarations

Conflict of Interest:

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest, or non-financial interest in the subject matter or materials discussed in this manuscript.

Ethical approval:

All procedures performed in studies involving human participants were in accordance with the ethical standards of our hospital's committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. And this article does not contain any studies with human participants performed by any of the authors.

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Figures

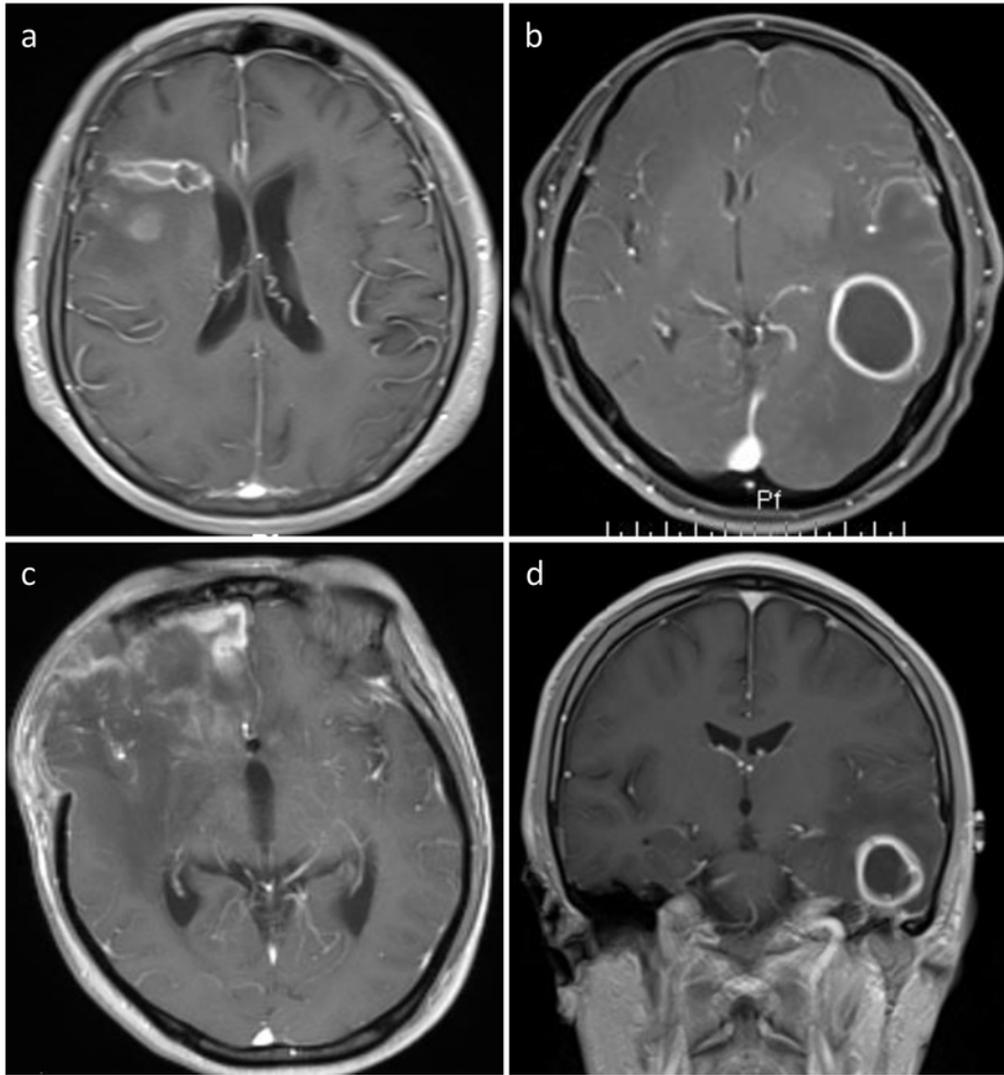


Figure 1

different kinds of brain abscesses: hematogenous multiple abscesses (a), cryptogenic solitary abscess (b), post-operative abscess (c), otogenic abscess(d)

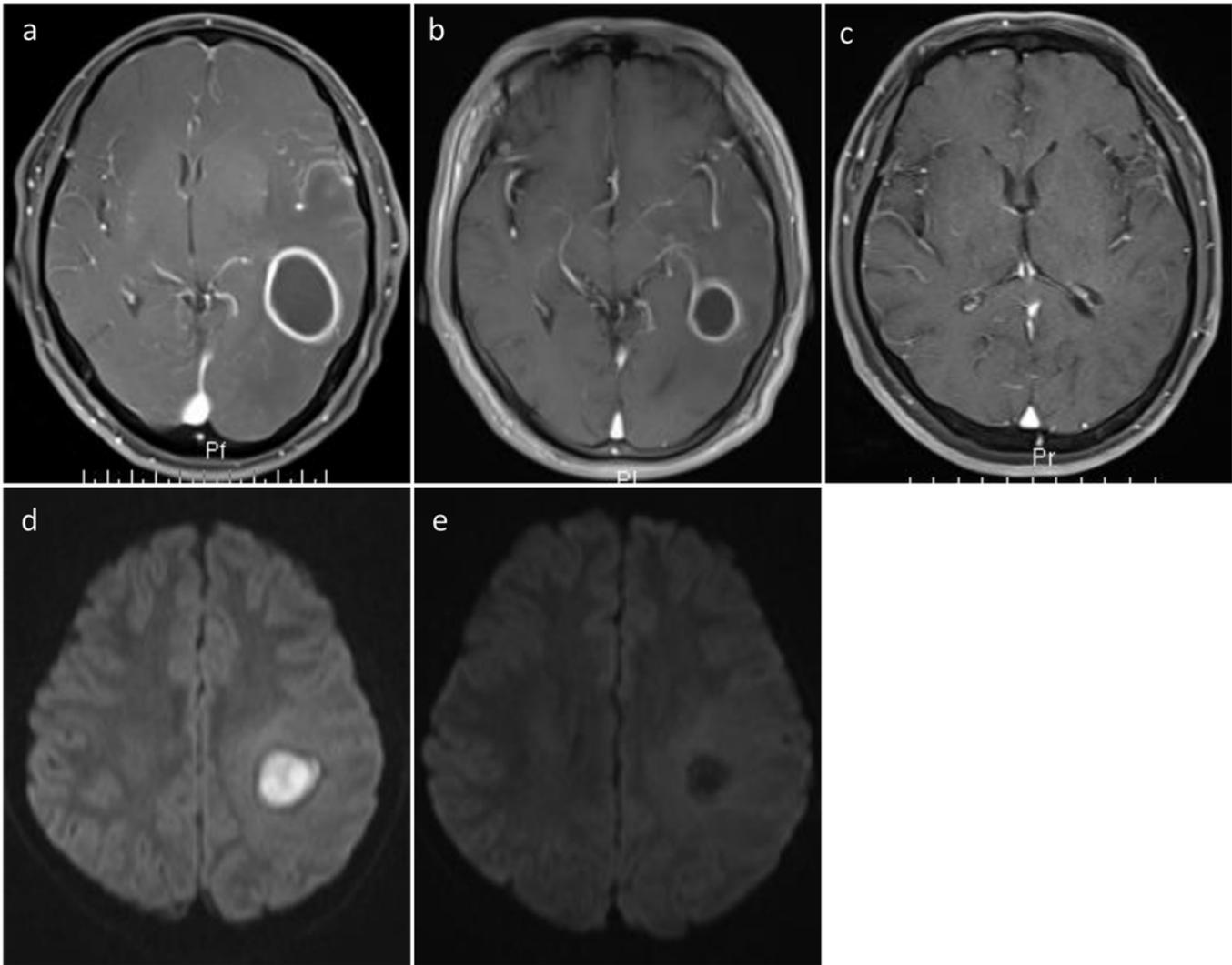


Figure 2

Typical neuro-imaging manifestation of brain abscess (BA): a-c) the manifestation of gadolinium-enhanced T1-MRI of temporal lobe brain abscess during the therapeutic process: a) before treatment; b) after a week of medicine therapy; c) six months later; d-e) diffusion-weighted imaging of brain abscess: d) the brain abscess showed high signal in DWI before treatment; e) after treatment the high signal turned into low signal in DWI.

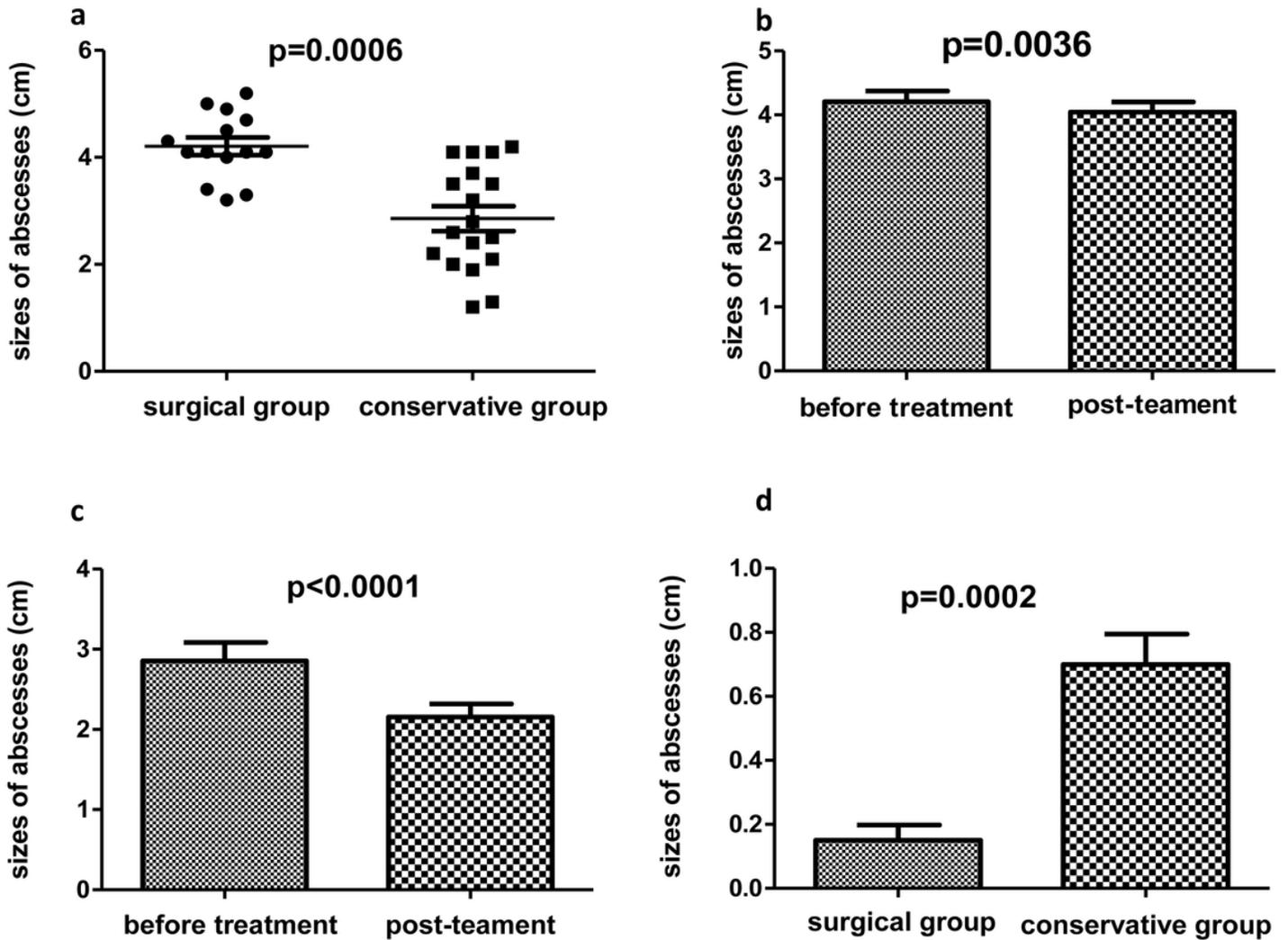


Figure 3

Comparison the abscess sizes between the surgical group and the conservative group before and after one week of treatment. a) Larger sizes of abscesses were measured in surgical group than the conservative group; b-c) the abscesses sizes declined obviously after a week of medicine therapy in surgical (b) and conservative groups (c); d) the extent of abscess sizes decline in conservative group was more significant than that in surgical group after a week of medicine treatment.

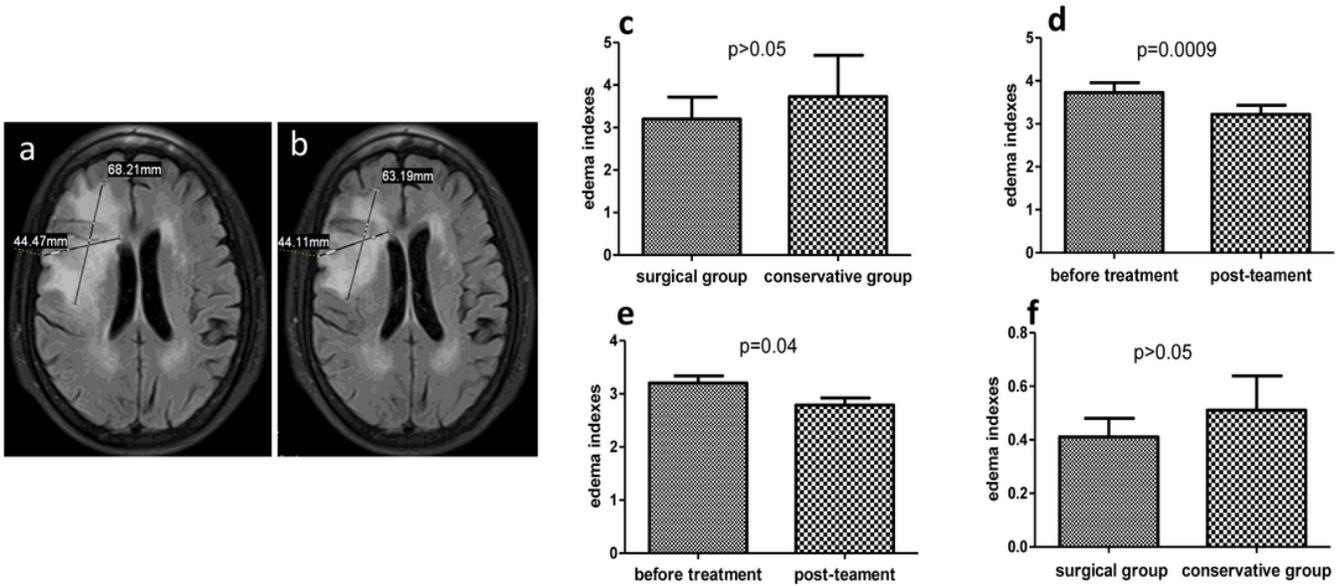


Figure 4

Comparison the EI (edema index) between the surgical treatment group and the non-surgical treatment group before and after one week of treatment: a, b) edema around the brain abscess relieved after a week of trial medicine therapy; c) the difference of abscess EI between the surgical group and the conservative group was not obvious before medical therapy; d-e) after a week of medicine therapy, though the abscess EI got a little decline in in conservative group (d) and surgical group (e), but the difference were not apparent; f) after a week of medicine treatment, the extent of EI decrease were not apparent different between the two groups.

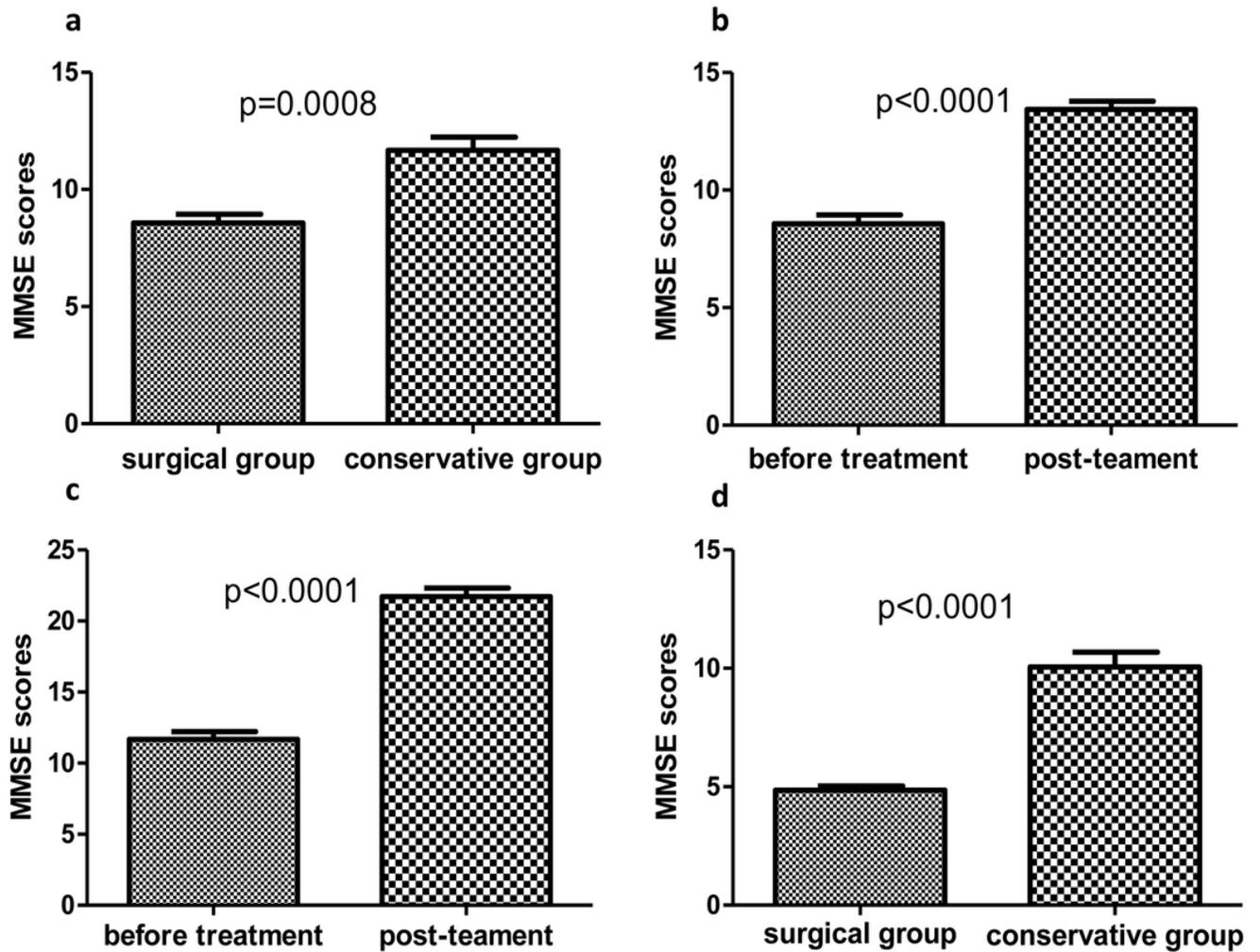


Figure 5

MMSE scores of the surgical treatment group and the non-surgical treatment group before and after one week of medical treatment. a) the conservative group had higher MMSE scores than the surgical group on admission; b-d) after one week of medical treatment, both the surgical group (b) and the conservative group (c) got an improvement in MMSE scores, but more significant MMSE scores enhancement were detected in conservative group (d).

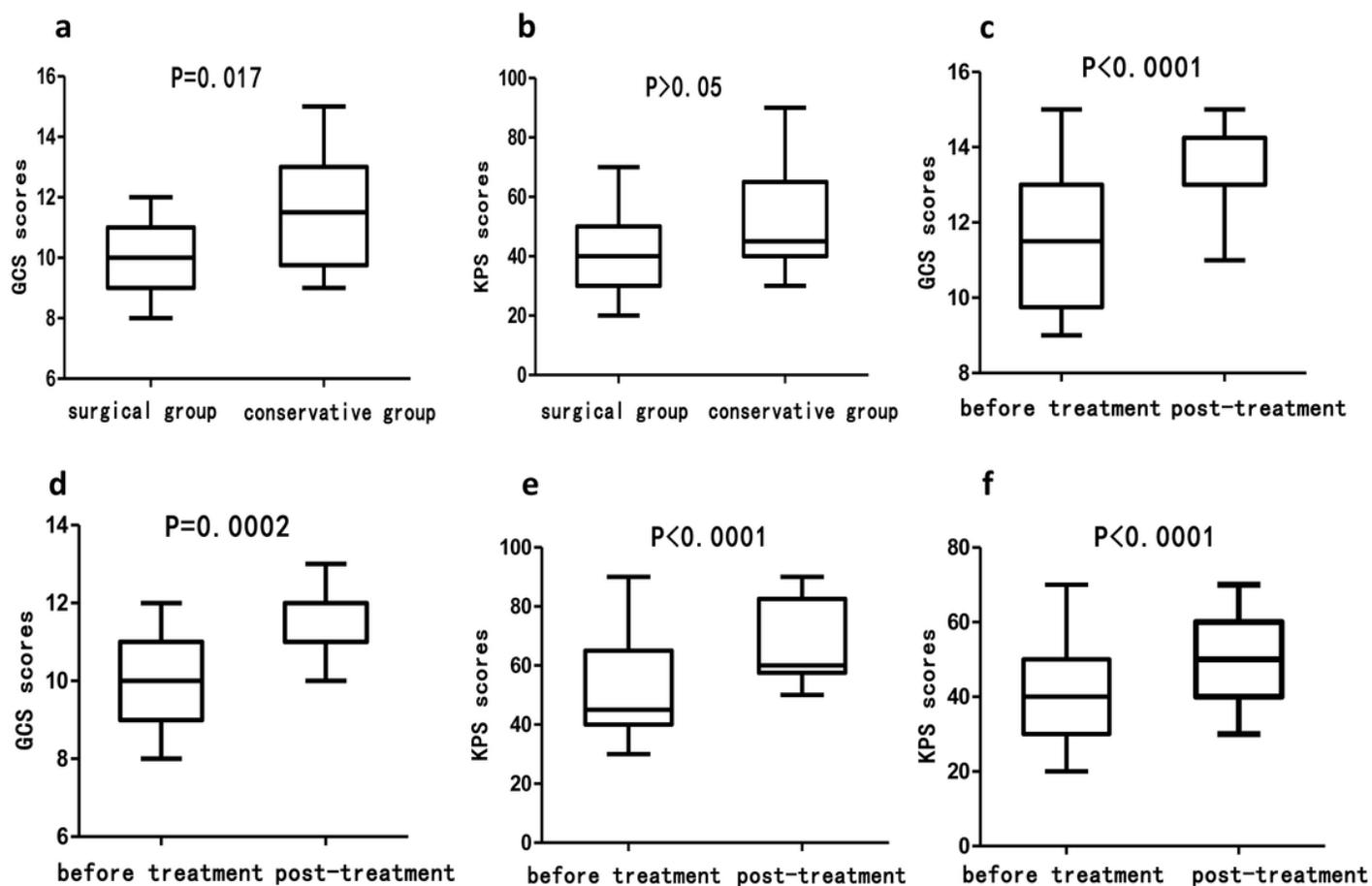


Figure 6

Comparison GCS and KPS between the surgical group and the conservative group before and after one week of treatment: a) the conservative group had higher GCS than the surgical group on admission; b-c) after a week of medicine therapy, GCS increased both in conservative group (b) and in surgical group (c); d) the conservative group had higher KPS than the surgical group on admission; e-f) after a week of medicine therapy, KPS increased both in conservative group (e) and in surgical group (f).

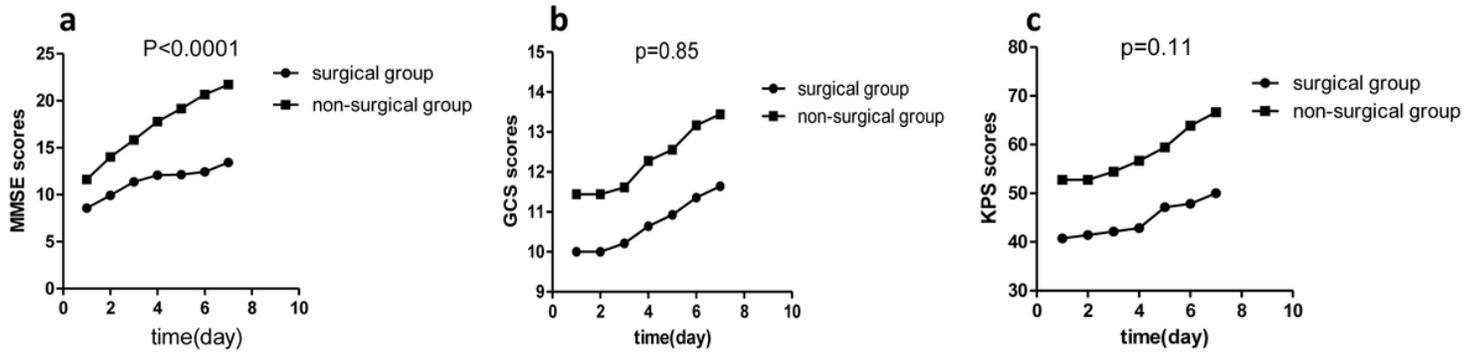


Figure 7

During one week of medical treatment, the consecutive variation of MMSE scores, GCS and KPS of patients were measured. (a) The consecutive variation of MMSE scores was more apparent in the conservative group than that in surgical group ($p < 0.0001$); b-c) the difference of the consecutive variation of GCS and KPS between the surgical group and the conservative group were not obvious ($p > 0.05$).

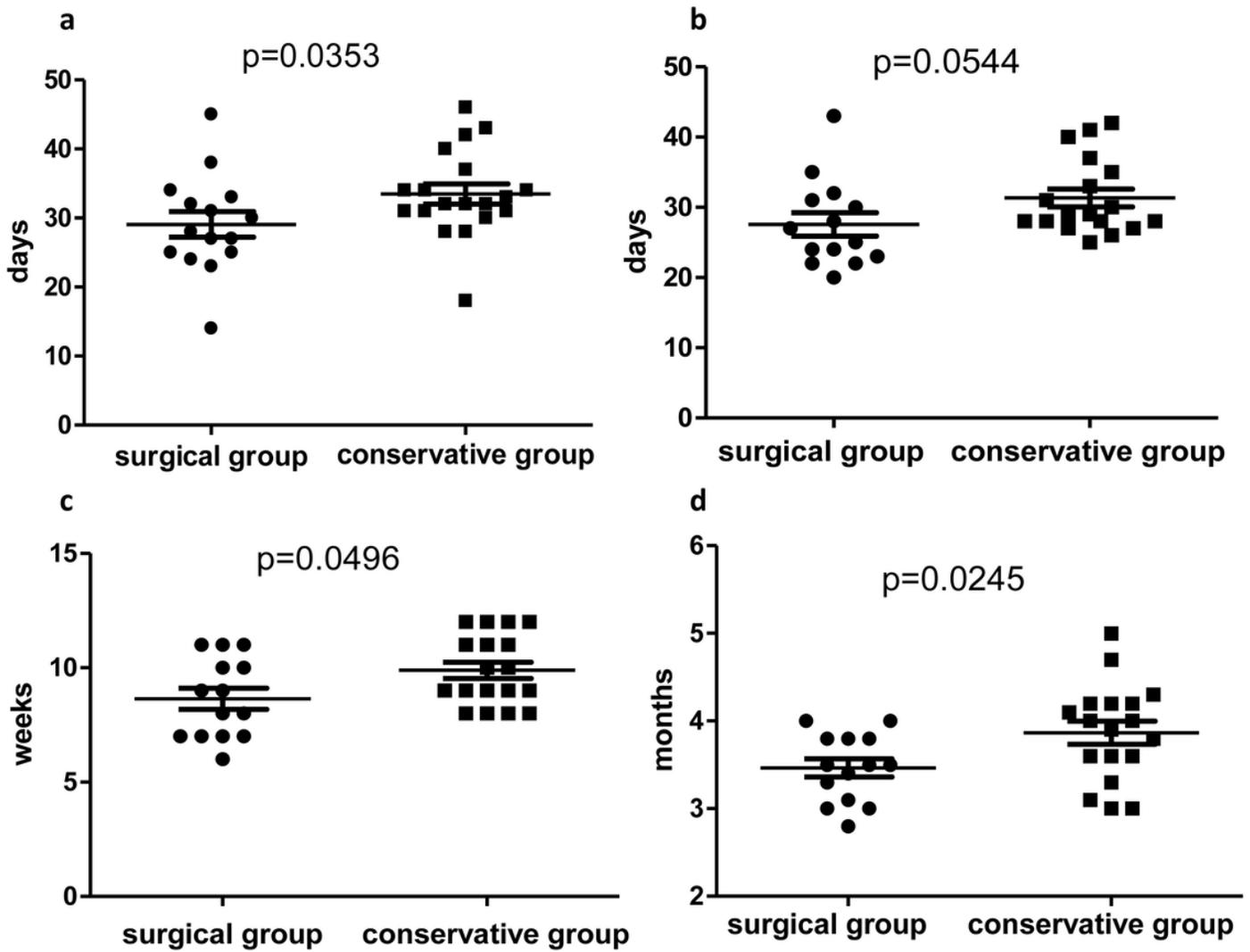


Figure 8

Differences of the whole treatment course between the two groups: a. conservative group had a longer hospital stays; b. the duration of Parenteral IV antibiotics was not obvious different between the two groups; c. conservative group had longer duration of oral antibiotics; d. surgical group could return to normal life Or work more quickly than conservative group.