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Notice

The Asian Medical Journal (AMJ) has changed its name to the Japan Medical Association Journal (JMAJ) from the April 2001 issue. The AMJ has been in publication for more than 40 years since its first issue. Its goal has been to promote medicine and health care mainly in Asia. Relevant articles were selected mainly from the Journal of the JMA and translated into English. It has been an academic journal containing the latest information in the field of medicine.

In conjunction with the change in the name, the journal's cover has been revised. The content of the JMAJ will continue to contain the latest information in medicine and health care in Japan, but it will be disseminated to medical-related organizations throughout the world, in addition to Asia. It will also contain information on JMA's activities and its stance on health care policies in Japan. Please note that the first issue of the JMAJ is volume number Vol. 44, No. 4 and the numbering continues consecutively from the previous AMJ issue. The ISSN 0004-461X will also continue to be the same. In addition, we are no longer accepting contributions to the AMJ or the JMAJ.

JMAJ Editorial Office

THE 52nd WMA GENERAL ASSEMBLY
Sheraton Grand Hotel
Edinburgh, Scotland
October 6, 2000

Inaugural Address as President of the World Medical Association

Eitaka TSUBOI, M.D.

President, World Medical Association
President, Japan Medical Association

Right Honorable Donald Dewar, Dr. Milton, Professor Blahos, Dr. Human, honored guests, ladies and gentlemen and fellow colleagues, it is a tremendous honor to be present at such a distinguished assembly as this and deliver my first presidential address as the new President of the World Medical Association. This is perhaps the brightest moment of my life. It is particularly fortunate at the junction of two centuries to be able to serve as President of the World Medical Association and work to improve human health and welfare. At the same time, I am also painfully aware of the great weight of responsibility that this position brings.

This honorable assembly has just witnessed my taking the highly dignified oath that I shall endeavor to assist all people to attain the highest possible level of health, and carry out the duties of the office of the President of the World Medical Association. I will remember this vow to the end of my days, a commitment to continue working with my esteemed colleagues from around the world.

I am very proud of the numerous declarations, statements, and resolutions that have been achieved by pooling the wisdom of the National Medical Associations. One example is the Declaration of Helsinki. In every country, this Declaration is reflected in laws and regulations, and I applaud its contribution to ensuring that physicians worldwide do everything in their power for their patients, within the principles of medical ethics.

One of the reasons I am particularly interested in the Helsinki Declaration is the issue of medical ethics and the mapping of the human genome, a technique that has developed quickly in recent years.

Humanity has made great strides toward unlocking the secrets of life itself at the end of the twentieth century. New treatments are being discovered for conditions that have until now been virtually untreatable, including many genetic diseases and cancer or even

This article is the inaugural address presented by Dr. Eitaka Tsuboi, President of the JMA when he took office as President of the World Medical Association at its 52nd General Assembly that was held in Edinburgh, Scotland on October 6, 2000.

diabetes, bringing hope to many people who have fallen into a spiral of despair. At the turn of the century, all humankind is waiting expectantly for the contributions to humanity that the mapping of the human genome may bring.

But at the same time we should remember some of the other important lessons that humanity learned in the twentieth century. Humans also succeeded in unlocking the secrets of the atom, thinking of the noble goal of improving human welfare, but instead ended up building a weapon of mass destruction.

This fatal weakness of human beings must not be realized again in the manipulation of the human genome. Genome mapping must be done for the sake of humanity, and as stated in the Hippocratic Oath, must "first do no harm." As members of the World Medical Association, we must use our collective wisdom to protect humanity in this way.

While we should be happy with the great fortune of being able to enjoy the benefits of unlimited progress in science and technology, I am also resolved that we should make a strong commitment to channeling the unlimited hopes that advanced research contains.

As President of the World Medical Association who bridges the old and new centuries, I will continue the basic commitment to medical ethics that the National Medical Associations have agreed to, beginning with the Helsinki Declaration, and base my presidency on the principle of "channeling the abundant benefits of advanced medical technology." This kind of principle will surely contribute greatly to progress in medical research. Although the benefits of advanced medical research are not limited to the results of human genome mapping, it is vital that medical researches contribute not only to finding cures, but also to ensuring patient safety.

In the increasingly productive field of clinical research, it is not easy, but we must also put our efforts into adequate consideration of the balance between high-quality results and patient safety. I believe that we must do so in order to give patients an increased sense of security, and reinforce their faith in the value of medical treatment itself. The theme of patient safety should also be an issue of special concern for the World Medical Association.

I also have great respect for the efforts of the World Medical Association to support physicians who are under pressure for various reasons. These efforts are vital from a moral standpoint as well. Whatever the conditions, the World Medical Association and its members stand by physicians in a weak position and lend support that at least eases their suffering. Such support also strengthens the World Medical Association as an organization, and thus increases the value of the World Medical Association in its other activities as well. In the future, it is important to further our support of physicians in need by making their cases known to the international community.

After the Ottawa General Assembly, Immediate Past President Dr. Blahos brought me a proposal for the creation of World Medical Association regional offices. This measure will produce many benefits including the ability to develop more concrete and more detailed

statements.

Work has already begun to establish the World Medical Association Asian Regional Office. In accordance with the report on the creation of regional offices, as modified by Chairperson of Council of the World Medical Association Dr. Milton and Secretary General Dr. Human, a proposal was made to the September 2000 Confederation of Medical Associations in Asia and Oceania Midterm Council Meeting to establish the Asian Regional Office in Tokyo. Establishing a network of regional medical offices, and developing their functions, will contribute greatly to the ability of the World Medical Association to further promote a healthy life for all people.

The World Medical Association also has a special interest in fostering the next generation of physicians. At the General Assembly, we invite representatives of medical students, and we should continue to do other such activities to deepen understanding of the World Medical Association and its goals. Furthermore, we should decide quickly on ways to reach out to them, and develop promotional materials and seminar programs to ensure that the next generation understands that at the heart of medical science and the practice of medicine is a love for humanity.

The Japan Medical Association celebrates the graduation of students from medical departments. As they embark on their journey into the world of medicine, the JMA presents them with a short essay by the renowned Japanese medical researcher Dr. Koan Ogata in which he reflects on "Die Verhaeltnisse Des Arztes" by German pediatrician Dr. Christoph Wilhelm Hufeland and wrote that the basic framework for all actions by physicians is a love for humanity.

Each national medical association probably has its own way of reaching out to the next generation, and if each NMA does this, I believe it will produce good results.

And even though it is already widely accepted that continuing education is essential for physicians, the World Medical Association can contribute by promoting widely the results of its deliberations and the common issues it has discussed. Wide dissemination of the work of the World Medical Association will help by both providing evidence of its success and providing a basis for development of further declarations and reports.

Finally, I would like to read for this assembly one of my favorite poems: "Strong in the Rain" by Kenji Miyazawa.

Kenji Miyazawa was born in the northeastern part of Japan. He lived his life in an extremely poor rural village, wrote fairy tales, and as a poet proclaimed his love for all of humanity. This poem is well-known in Japan.

STRONG IN THE RAIN

Strong in the rain
Strong in the wind
Strong against the summer heat and winter snow
He is healthy and robust
Unselfish
He never loses his temper
Nor the quiet smile on his lips
He eats four small bowls[i] of unrefined rice[ii]
Miso[iii] and a small portion of vegetables each day
He does not consider his own interest
In whatever occurs...his understanding
Comes from observation and experience
And he never loses sight of things
He lives in a little thatched-roof hut
In a field in the shadows of a pine tree grove
If there is a sick child in the east
He goes there to nurse the child
If there's a tired mother in the west
He goes to her and carries her sheaves
If someone is near death in the south
He goes and says, "Don't be afraid"
If there's strife and lawsuits in the north
He demands that the people put an end to their pettiness
He weeps at the time of drought
He plods about at a loss during the cold summer
Everyone calls him "Blockhead"
No one sings his praises
Or takes him to heart
He is the sort of person
I want to be

[i] The Japanese measurement translated here is "go", about 0.04 liters of rice.
[ii] Unrefined, or unpolished rice, was considered to be fit only for the poorest people in Japan.
[iii] Miso is a common soup base in Japan made from fermented soybean paste and salt.

Indications for Total Knee Arthroplasty and Choice of Prosthesis

JMAJ 44(4): 153–158, 2001

Hiroomi TATEISHI

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Abstract: Total knee arthroplasty (TKA) is performed when the knee joint is severely damaged in osteoarthritis, rheumatoid arthritis and other diseases. In Japan, about 20,000 TKA procedures are performed each year and it is the second most common arthroplasty after total hip arthroplasty (THA). Knee replacement prostheses can be classified into three categories, which are unconstrained, semiconstrained, and constrained. Depending on the underlying disease and the extent of destruction of the knee joint, a prosthesis is selected. At present, semiconstrained prostheses are most commonly used. This type of prosthesis can be divided into groups depending on whether surgery requires excision of the posterior cruciate ligament and whether the prosthesis has posterior stabilizer or not. A prosthesis that can be implanted while sparing the posterior cruciate ligament is most commonly employed. When the knee is severely damaged and unstable, however, a stabilised prosthesis is used. Unconstrained prostheses are used for unicompartmental knee arthroplasty. Constrained prostheses are used for revision arthroplasty and for arthroplasty in knees that are extremely unstable, although the employment of this type is rare. Thus, a prosthesis is chosen depending on the underlying disease and the extent of destruction of the knee along with consideration of the general health and the blood supply to the lower extremity.

Key words: Knee prosthesis; Total knee arthroplasty; Osteoarthritis; Rheumatoid arthritis; PCL-sparing arthroplasty

Introduction

Total knee arthroplasty has been most commonly performed for severe knee joint damage in patients aged 60 and over. The replacement prosthesis of choice varies depending on the underlying disease, the severity of knee joint damage, and the age of the patient. The indications for total knee arthroplasty are discussed in this article based on the underlying disease and the extent of knee damage together with a description of the various types of prosthesis.

This article is a revised English version of a paper originally published in the Journal of the Japan Medical Association (Vol. 123, No. 4, 2000, pages 470–474).
The Japanese text is a transcript of a lecture originally aired on October 26, 1999, by the Nihon Shortwave Broadcasting Co., Ltd., in its regular program “Special Course in Medicine”.

Table 1 Types of Knee Prostheses

1. Unconstrained
   Modular type-Marmor, Lotus, Savastano polycentric type (for unicompartmental knee arthroplasty)
2. Semiconstrained
   Many prostheses fall into this category, including the geomedic, anametric, total condylar, kinematic, Kodama-Yamamoto, ceramic devices and others. (Prostheses implanted with preservation of the posterior cruciate ligament, prostheses implanted with excision of the posterior cruciate ligament, and stabilised prostheses.)
3. Constrained
   Walldius, Shiers, Guépar, Kinematic rotating hinge

Types of Knee Prosthesis

Total knee arthroplasty is usually performed in patients aged 60 years or older when the bone and articular cartilage are so severely damaged that there is no other effective therapy. The common diseases causing knee damage treated by arthroplasty are osteoarthritis, chronic rheumatoid arthritis, and osteonecrosis, while contraindications for knee arthroplasty include purulent arthritis and tuberculosis.

Knee prostheses can be classified into three major types, which are unconstrained, semiconstrained, and constrained. Like an endoprosthesis for unicompartmental knee arthroplasty, an unconstrained device is used to replace only a very small portion of the articular surface or a very thin surface layer of tissue, leaving the anatomical structure of the joint intact. A semiconstrained prosthesis is also used for superficial joint replacement. There are two types of semiconstrained devices. One requires excision of the posterior cruciate ligament, whereas the ligament is spared by the other type. In Japan, the posterior cruciate-sparing type of semiconstrained prosthesis is most frequently used. Among the prostheses requiring excision of the posterior cruciate ligament, the stabilised prosthesis, which facilitates the acquisition of anteroposterior stability of the knee, is used most frequently.

In the United States, however, stabilised prostheses that require excision of the posterior cruciate ligament have been used most commonly, possibly because of the different health care system from that in Japan. The constrained type of prosthesis is only indicated for knees that are very unstable because of large bone defects or for revision total knee arthroplasty. A prosthesis of this type consists of a tibial component and a femoral component, which are connected by a hinge, and it allows reconstruction of a stable knee.

Fixation of Knee Prostheses

To fix each component of a prosthetic joint to the bone, there are two possible methods. Methyl methacrylate bone cement can be used as one method, whereas screws are used along with metal beads or hydroxyapatite granules in uncemented fixation. The beads or granules are applied to the bone surface under the prosthesis.

If the patient is relatively young and the bone is strong, as occurs in osteoarthritis, uncemented fixation is useful. In patients with rheumatoid arthritis or osteoporosis, however, the bone is often fragile and uncemented fixation frequently results in subsidence or loosening of the implant. Consequently, cemented fixation, which allows early resumption of weight bearing and achieves a better outcome, is useful for such patients.

There is also hybrid fixation, which is a combination of cemented and uncemented fixation. In hybrid fixation, either the femoral or tibial component is fixed with bone cement, while the other component is fixed without cement. Usually, uncemented fixation is used for the femoral component, while the tibial component is cemented.

Osteoarthritis

The most common disease of the knee is

osteoarthritis. This is initially treated by rehabilitation (exercise), thermotherapy, topical medications (moist packs), and wearing of a supporter, while the course is being followed. Additional conservative management includes using a plate under the sole to raise the lateral border of the foot, and intraarticular injection of agents such as hyaluronic acid to protect the cartilage. Symptoms unresponsive to such conservative treatment are an indication for surgery. Osteotomy and knee arthroplasty are indicated for younger and older patients, respectively.

In more than 95% of Japanese patients with osteoarthritis of the knee, deformity of the bone and articular cartilage predominantly affects the medial compartment. This type of osteoarthritis is usually treated by high tibial osteotomy if the patient is relatively young, while unicompartmental knee arthroplasty (UKA) or total knee arthroplasty is indicated for patients aged 65 to 70 years or older.

Unicompartmental knee arthroplasty (UKA) involves replacement of the affected articular surfaces in the medial compartment (distal femur and proximal tibia) using metal or ceramic components, with retention of both the anterior and posterior cruciate ligaments. UKA of the knee is indicated for osteoarthritis or osteonecrosis in patients between 65 and 70 years old or older. It is contraindicated for rheumatoid arthritis or other inflammatory diseases because the bone and cartilage lesions can be expected to spread and eventually the entire knee will be involved. Because both the anterior and posterior cruciate ligaments are spared, neither ligament can show degeneration and the knee must be completely stable or minimally unstable.

When UKA is considered, the weight of the patient is the most important factor and obesity is a contraindication. It is our general rule that this method is contraindicated for patients exceeding 70 kg in weight. In the United States, however, some surgeons use 90 kg as the cutoff value. A body mass index (BMI: weight (kg) / height $(m)^2$) exceeding 25 or 27 is considered to indicate mild obesity and obesity, respectively. It is desirable for this index to be below 25. The mean BMI exceeded 25 in 50 patients who underwent total knee arthroplasty recently at our department. It cannot be denied that patients tend to be obese when their osteoarthritis is so advanced that it requires surgical treatment.

UKA of the knee has several advantages: 1) It only takes a short time to perform, 2) postoperative rehabilitation can be started earlier and proceeds smoothly, and 3) the surgical invasion is smaller and there is little risk of postoperative infection. If the patient is overweight, the prosthesis will subside over time postoperatively and then will become loose. Consequently, the weight should be controlled quite strictly.

If the bones and cartilage of the entire knee joint have been affected, as occurs in advanced osteoarthritis, total knee arthroplasty is indicated instead. Precisely speaking, if flexion of the knee is reduced because of severe genu valgum or varum and there is a prominent fixed flexion contracture, total knee arthroplasty is the treatment of choice. If genu varum is prominent and the knee is stiff, total knee arthroplasty rather than UKA is also indicated, even if the patient's osteoarthritis shows medial predominance. When the range of motion of the knee is severely restricted by flexion contracture, excision of the posterior cruciate ligament becomes necessary. Consequently, total knee arthroplasty is indicated.

When patients with osteoarthritis have strong bones without osteoporosis and are around 60 years old, instead of fixation using bone cement, quite a few surgeons employ uncemented fixation using screws that are coated or treated with hydroxyapatite. Bone cement has systemic effects, such as causing hypotension. Also, a great deal of heat is generated during polymerization and this can damage tissues around the site of fixation. However, Ranawatt *et al.* studied the results at

more than 20 years after cemented total knee arthroplasty in the United States and found that the outcome was excellent in more than 90% of patients, suggesting that bone cement causes little harm. Moreover, patients benefit from the use of cement because it achieves firm fixation soon after the operation and hence allows the knee to bear weight earlier, allowing the patient to start rehabilitation more rapidly.

It is still controversial whether the articular surface of the patella should be replaced with a polyethylene patellar component in total knee arthroplasty. According to my experience, several years after total knee arthroplasty without patella replacement, a number of patients will require additional patellar replacement because of local pain. Consequently, patellar replacement is performed with the initial total knee arthroplasty at our department. Particularly in patients who have chronic rheumatoid arthritis, it may extend to involve the articular surface of the patella, and the disease has recurred this way in some of our patients. Thus, patellar replacement seems to be necessary when the underlying disease is rheumatoid arthritis.

If the knee shows anteroposterior instability because of severe degeneration of the anterior and posterior cruciate ligaments or because of marked varus or valgus deformity, such instability may persist after joint replacement if the cruciate ligaments are spared and postoperative rehabilitation will be impaired.

Stabilised knee prostheses are equipped with a stabiliser that increases the anteroposterior stability of the knee joint and are useful for unstable knees like those described above. If the width of the stabiliser is increased, it can also prevent instability in the frontal plane. To implant a posterior-stabilised knee (PSK) prosthesis, the posterior cruciate ligament is divided from the femur at its insertion into the periosteum, and osteotomy is done to create room for the stabiliser between the femoral condyles. Because osteotomy is required for the PSK prosthesis, posterior cruciate ligament-sparing arthroplasty with a prosthesis that does not need osteotomy is more commonly performed in Japan. However, the reasons for selecting prostheses vary between countries, and use of the PSK prosthesis is far more common in the United States.

Excision of the posterior cruciate ligament when inserting the PSK prosthesis allows adequate division of the soft tissues behind the knee, which makes it easy to pull the proximal articular surface of the tibia anteriorly during the operation and assists surgical manipulation. The space that remains even after insertion of the polyethylene tibial plate makes it easy to achieve flexion of 90 degrees or more by postoperative rehabilitation. The roll-back that occurs during flexion of the knee is believed to be physiological when the posterior cruciate ligament is intact. In many cases, however, the posterior cruciate ligament shows degeneration to some extent at the time of arthroplasty. In addition, there is often scar tissue behind the knee and the division of such scar tissue for insertion of a PSK prosthesis is said to allow physiological roll-back. This view is partly based on the finding that wear of the polyethylene tibial component is greater after posterior cruciate-sparing arthroplasty than after PSK arthroplasty.

In the United States, patients are only hospitalised for 3 or 4 days after total knee arthroplasty. Following discharge, they perform rehabilitation exercises at home by themselves, so there is a possibility that they will stop exercising if they feel pain, even if it is slight. According to a recent report from the United States, as many as 40% of the patients who underwent total knee arthroplasty with sparing of the posterior cruciate ligament required manipulation under anaesthesia about 1 month postoperatively to mobilize the knee because exercise at home had failed to achieve flexion exceeding 90 degrees. When the PSK prosthesis was used, in contrast, few

patients required this additional procedure. This indicates that with the PSK prosthesis, postoperative exercise at home can achieve adequate flexibility of the knee, which is considered to be one reason for its popularity in the United States.

Chronic Rheumatoid Arthritis

In rheumatoid arthritis, articular damage caused by inflammation involves the entire knee joint. In many patients, not only the anterior cruciate ligament, but also the posterior cruciate ligament, undergoes degeneration because of inflammation. The anterior cruciate ligament is completely covered by the synovial membrane and so is more susceptible to damage by synovial inflammation. When inflammation is severe, the whole anterior cruciate ligament can disappear in some cases. In the case of the posterior cruciate ligament, only the anterior segment is covered by synovial membrane and the posterior segment is bare so it is thought to be less liable to degenerate than the anterior cruciate ligament. However, if inflammation is severe in patients with rheumatoid arthritis, the posterior cruciate ligament is always affected. Consequently, its excision and removal of the affected synovial membrane and scar tissue behind the knee is useful because it prevents the recurrence of inflammation.

In patients with rheumatoid arthritis, osteoporosis of the bones around an affected joint becomes severe because of inflammation and reduced movement. Because of the presence of osteoporosis, we always use bone cement to fix implants in rheumatoid arthritis patients.

When there is a large bone defect in either the medial or the lateral condyle of the tibia, it will remain if the bone is cut in the conventional manner. Therefore, the defect must be repaired with bone grafts using bone fragments obtained by femoral osteotomy. Recently, such defects have also been repaired by inserting a metal wedge that is fixed with bone cement.

Constrained Knee Prostheses

When the knee has large bone defects or marked instability that cannot be repaired with a resurfacing prosthesis, or when revision arthroplasty is performed because of loosening or subsidence of the previous implant, constrained prostheses are used. The early hinged prostheses did not permit the knee to rotate at all and hence placed excessive stress on the stem of the implant when the knee joint moved, frequently leading to destruction of bone around the tip of the stem. Consequently, prostheses of this type are no longer used. The current hinged prosthesis is called a rotatory prosthesis and it can rotate around the axis of the stem of the tibial component. This type of prosthesis is associated with fewer complications such as loosening.

Complications of Knee Arthroplasty

The major complications of knee arthroplasty are mechanical problems, such as loosening and subsidence of the prosthesis, and postoperative infection. Infection occurs immediately after implantation in some cases, but it is often delayed and manifests several years after surgery. Although the incidence of infection varies among institutions, it is usually around 1–2%.

Once it has become infected, a prosthesis must be removed. However, removal means that the patient will be unable to perform normal daily activities because of instability of the knee, the reduced length of the affected limb, and the device worn to compensate for knee instability. Therefore, great care must be taken to prevent infection and this cannot be overemphasized.

Immunosuppressants such as methotrexate (MTX) are used in the treatment of rheumatoid arthritis. There is a risk that such drugs

could affect the immunity of patients and reduce their resistance to infection, so withdrawal for a period before and after surgery warrants consideration. Patients with diabetes and patients on hemodialysis have a high risk of developing infection. It is therefore better to choose the arthroplasty associated with the least surgical, if possible.

Summary

The indications for knee arthroplasty and the types of prosthesis were described above. In patients with osteoarthritis, it is desirable for the amount of bone removed at arthroplasty to be minimized and the posterior cruciate ligament to be spared if it is in good condition. In patients with rheumatoid arthritis, however, there is usually severe osteoporosis and severe degeneration of both cruciate ligaments causing the knee to be unstable, so a PSK prosthesis is used and is fixed with bone cement.

For revision arthroplasty, a constrained knee prosthesis of the rotatory hinged type seems to be most suitable, because the knee is severely unstable and there is considerable bone loss. Among the complications of knee arthroplasty, infection is the most serious and its prevention deserves great care. Once a prosthesis is infected, the patient will suffer serious disability in daily life. Risk factors for infection should be countered with great diligence whenever possible.

Indications for Total Hip Arthroplasty and Selection of Prosthesis

JMAJ 44(4): 159–164, 2001

Hirokazu IIDA

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Abstract: The initial clinical success of total hip arthroplasty was confirmed more than 30 years ago and it is now considered as one of the most useful orthopedic procedures. With regard to the long-term outcome of this surgery, the 20-year prosthetic survival is 83% and 10-year survival rates of almost 100% have occasionally been reported. New hip replacement prostheses are still being developed, but the use of a new prosthesis requires adequate knowledge and caution because its value can only be established after testing for more than ten years and it is not uncommon to find new defects during the testing process. To select a prosthesis, various factors should be taken into consideration, including the method of fixation (cemented or cementless), the combination of articular surfaces, the quality and morphology of the patient's bones, and the surgeon's experience. When the patient is young, it is important to consider total hip arthroplasty as part of a long-range therapeutic plan including revision arthroplasty, which can follow a course of over 30 years.

Key words: Total hip arthroplasty; Indication; Bone cement; Polyethylene; Component

Introduction

Charnley's original total hip arthroplasty procedure, developed about 35 years ago, was a breakthrough on which the current success in this field depends (Fig. 1). Charnley placed priority on the development of low-friction surfaces that allowed articular motion with a low torque and called his prosthesis a low-friction arthroplasty. The design that he created was typically a combination of a small femoral head (about 22 mm in diameter) and a polyethylene socket. He also developed various revolutionary surgical techniques for the performance of arthroplasty, leading to clinical success.

Subsequently, many other types of prosthesis have been developed for total hip arthroplasty, with the aim of achieving better results. These prostheses were improved in some

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The Japanese text is a transcript of a lecture originally aired on October 28, 1999, by the Nihon Shortwave Broadcasting Co., Ltd., in its regular program "Special Course in Medicine".

Fig. 1 Charnley total hip arthroplasty

respects, but many of them were eventually abandoned because new drawbacks were detected.

Even more than 30 years after Charnley's success, new prostheses are continuously being developed. A surgeon who wants to use such a new prosthesis should select it on the basis of extensive knowledge and must exercise caution, because the testing for more than 10 years that is necessary to assess its clinical value has not usually been completed. Therefore, it is not rare for different surgeons to choose different prostheses for the same indication even if the selection is based solely on consideration of functional advantages. When a prosthesis is chosen, however, factors related to the patient and the surgeon should be taken into consideration as well as its function. Thus, the prosthesis chosen will differ between patients and surgeons. Various total hip replacement prostheses are currently available and it is impossible to deal with all of them in this article. In addition, there is not necessarily a consensus among surgeons about the indications for each prosthesis. Therefore, the following article will mainly explain the most common views in a systematic manner.

The Durability of Total Hip Prostheses

How long can the current total hip arthroplasty components last? This question is not easy to answer. In a multicenter follow-up study of Charnley's total hip arthroplasty involving about 5,000 patients, 83% of the primary implants were effective for at least 20 years.[1)] If this is defined as the 20-year survival rate for hip prostheses, then the recent 10-year survival rate is 97–98%, indicating that total hip arthroplasty has become extremely successful.[2,3)] Consequently, prostheses that are selected for clinical use should have an expected life exceeding this period and those which are less durable should not be used.

Types of Hip Prostheses

A total hip prosthesis usually consists of two components, a socket that is fixed to the acetabulum and a stem that is inserted into the femur. In addition, there is another type called a monopolar or bipolar prosthesis comprising a single component or a femoral head alone with no acetabular component.

The method of fixation can be classified as follows; 1) cemented, 2) cementless, and 3) hybrid. In the third category, each of the two components is fixed to the bones in different ways. Further classifications based on the materials and surface of each component are possible.

With respect to the type of articular surface, the combination of an ultra-high molecular weight polyethylene socket and a metal or ceramic femoral head is the most common. Metal-metal and ceramic-ceramic combinations have also been developed recently.

To determine the indications for each type of prosthesis, the following factors should be taken into consideration.

With the monopolar prosthesis, in which the

femoral stem and head are united, both components move as one. The prosthetic femoral head articulates with the patient's acetabulum to reconstruct a functional joint. This type of joint replacement was developed about 50 years ago. Consequently, it has been tested for about 50 years in clinical use. It is structurally simple and produces little wear debris, a cause of osteolysis. Despite these advantages, there is a possibility of the acetabular cartilage and bone being worn away by mechanical friction, leading to migration of the prosthetic head.[4] The majority view seems to be that use of this type of prosthesis is currently limited to fractures of the femoral neck in relatively inactive elderly patients. Low cost may be another reason to choose this type, because it is less expensive than bipolar prostheses as described below.

A B

Fig. 2 Bipolar prosthetic femoral head

The bipolar prostheses are discussed next (Fig. 2). The first bipolar prosthesis was developed about 25 years ago in order to overcome the drawbacks of the monopolar prosthesis.[4] The bipolar prosthesis, which has two functional joints, is also called a dual-bearing type. In other words, the prosthetic femoral head consists of two parts, the outer surface of the outer part articulates with the patient's acetabulum, while the inner surface articulates with the core of the prosthetic femoral head via bearings that lie between them.

Because the motion allowed between the acetabulum and the outer surface of a bipolar prosthesis is smaller compared with that between the acetabulum and a monopolar prosthesis, it was expected that migration of the prosthetic femoral head would also be suppressed. In fact, hemiarthroplasty with a bipolar hip prosthesis for fractures of the neck of the femur and necrosis of the femoral head was found to be successful if the acetabular cartilage had been preserved. Consequently, bipolar hip prostheses are used widely at present. In patients with osteoarthrosis of the hip, bipolar hip arthroplasty was also used instead of standard total hip arthroplasty. The outcome was initially excellent. At 10 years or more after implantation, however, migration of the femoral head showed a high incidence. Moreover, osteolysis due to wear debris from the articular surface has been recognized.[5] Bipolar hemiarthroplasty was performed for relatively young patients at first because revision was thought to be easy. However, the frequent occurrence of migration of the femoral head made this procedure less beneficial than total hip arthroplasty with regard to preservation of the acetabular bone. This seems to be the current consensus.

The main subject of this article is total hip arthroplasty, and the indications for this procedure will be discussed under various categories.

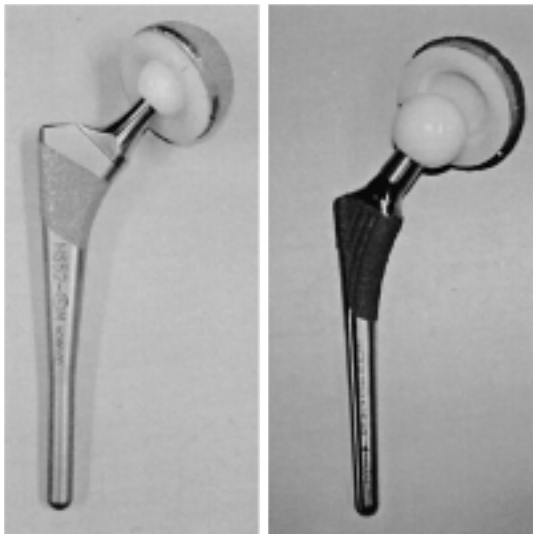
There are two major techniques of fixation, which are cemented (Fig. 3) and cementless (Fig. 4). The method that should be chosen is one of the most controversial issues even among experts.

Cemented fixation has various advantages. In general, rigid fixation can be obtained immediately after the operation, this technique can be applied despite variations in the

A B

A: Articular surfaces;
alumina-ceramic and ultra-high molecular weight polyethylene
B: Articular surfaces;
zirconia-ceramic and ultra-high molecular weight polyethylene

Fig. 3 Total hip joint prosthesis for cemented fixation



A B

A: Articular surface;
zirconia-ceramic and ultra-high molecular weight polyethylene
B: Articular surface;
alumina-ceramic and alumina-ceramic

Fig. 4 Total hip joint prosthesis for cementless fixation

morphology and properties of the bone, and the interface produced by cemented fixation is resistant to the penetration of wear debris. However, several drawbacks have been also recognised. The outcome varies considerably depending on whether or not the intraoperative cementing process is successful, rarefaction of the adjacent bone is often accelerated if the prosthesis becomes loosened, the cement may be difficult to remove at revision hip arthroplasty, and fixation of the socket is inferior to that of the stem.

The advantages of cementless fixation include extremely rigid fixation if bone growth into the pores of the surface coating occurs, relatively good preservation of bone mass even if loosening occurs, and the fact that revision arthroplasty can be performed without removing cement. Drawbacks include possible contraindication when the bone is inappropriate, occasional poor fixation due to subsidence of the implant or for other reasons when the initial fixation is insufficient, more common occurrence of osteolysis due to wear debris than after cemented fixation,[6] the potential extreme difficulty of extracting an implant that is firmly fixed, and the possible persistence of femoral pain. Regardless of the method of fixation, an implanted prosthesis causes mechanical stress on the bone to become nonphysiological. Consequently, the bone around the implant may undergo atrophy, rarefaction, or hypertrophy during the long postoperative course.

The selection of a method for fixation should not only be based on durability and functional advantages, but also on the countermeasures available for coping with complications or revision in the future. In other words, the surgical procedure to be used for revision, the extent of invasion, and the method of handling bone defects should all be taken into consideration when a technique for fixation is selected.

The following section discusses prostheses using a classification based on the type of articular surface. Because the methods of fixation have gradually been improved, some

researchers now consider that the longevity of artificial joints depends on the rapidity and severity of wear.[6] Even if excellent fixation is obtained after total hip arthroplasty, the bone around the implant begins to undergo osteolysis from 10 years or more after the operation and this may result in loosening. It has been clarified that the major cause of osteolysis is wear debris from the polyethylene covering the articular surface.

Several attempts have been made to prevent this osteolysis, including improvement of the articular surface of the femoral head by a better polishing technique, the use of an alumina or zirconia ceramic head in place of the conventional metal head, improvement of the resistance to frictional wear by using polyethylene with a higher molecular weight and intermolecular crosslinking, and the use of a ceramic or metal socket in place of polyethylene to produce a ceramic-ceramic (Fig. 4B) or metal-metal combination prosthesis, respectively. The long-term outcome is already known for some of these methods.

With a ceramic-ceramic prosthesis, although there are few wear debris, the long-term outcome is no better than that for the conventional prosthesis.[7] This suggests that the material used in place of the conventional polyethylene to reduce wear may alter the physical properties of the implant such as the friction coefficient and the rigidity of fixation. Thus, attempts at improvement cannot accomplish their goal unless the reconstructed joint is well-balanced. Recent research has indicated that remarkable progress may be achieved regarding this problem in the near future.

Patient Factors

When total hip arthroplasty is indicated, a prosthesis is selected by taking the patient's age and underlying disease into consideration because the properties and morphology of the host bone will depend on these factors.

With regard to selection based on the patient's age, usually cementless fixation is indicated for relatively young patients and cemented fixation for elderly patients. Because younger patients are more active and often require revision in the future, cementless fixation, which allows rigid fixation with the possibility of preserving the bone mass, is chosen. This policy is not absolute, however, and the possibility of osteolysis and difficulty of removing the implant at revision should be considered.

When the patient has osteoporosis, e.g., patients with rheumatoid arthritis and elderly patients, cemented fixation is usually considered more appropriate because the cementless method often fails to achieve rigid initial fixation. When the acetabulum and the femur are small and deformed as in patients with congenital acetabular dysplasia, reconstruction by a cementless technique is sometimes difficult and cemented fixation may be better. The selection procedure described above is generally applicable. However, some surgeons have employed different selection criteria based on various modifications invented for particular purposes.

Factors Related to the Surgeon

If arthroplasty is performed with a new prosthesis that the surgeon is using for the first time, it is difficult to accomplish the operation perfectly, no matter how skilful the surgeon may be. Even though different prostheses are available for different indications, if there are too many choices, the surgeon's experience with a particular prosthesis may be inadequate. It is often difficult to fully understand the advantages and drawbacks of a certain type of prosthesis without sufficient clinical experience.

For example, cemented fixation requires considerable skill to achieve an excellent result. With the cementless technique, the rigidity of fixation depends on the size of the prosthesis selected and experience in using the

surgical instruments. Consequently, using too many types of prostheses for different conditions is not a good method of maintaining the outcome of arthroplasty at a high standard. It seems to be more appropriate to choose one prosthesis with which the best long-term results are achieved as the main type and also provide one or two additional options.

Conclusion

The earliest clinical success with total hip arthroplasty was confirmed more than 30 years ago and the value of total hip arthroplasty as one of the most useful therapeutic procedures in the orthopedic field has been established. With respect to the long-term outcome, a 10-year prosthetic survival rate of nearly 100% has been reported occasionally. Not only improvement of instruments, but also attempts to maintain a certain standard for individual operations based on the training of surgeons needs to be considered.

In conclusion, I would like to emphasize the necessity of considering the prolonged postoperative course over 30 years or more and the need for revision arthroplasty, particularly when total hip arthroplasty is indicated for young patients.

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Complications of Total Hip Arthroplasty and Their Prevention and Management

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Abstract: The complications of total hip arthroplasty are described and treatment is discussed for the following six problems: Postoperative dislocation, femoral fracture, deep infection, heterotopic ossification, aseptic loosening of components, and deep vein thrombosis and/or pulmonary embolism. Postoperative dislocation and deep infection usually occur in the early postoperative period. Good technical skill and careful attention to the prevention of infection are extremely important. The major complications requiring revision are periprosthetic fracture, deep infection, and aseptic loosening of components. In such a situation, the surgeon again needs sufficient technical skill and considerable experience. Ectopic bone formation occurs more frequently in Japanese patients than has been realized previously. Uncemented THA is probably associated with a high rate of ectopic bone formation. Deep vein thrombosis and pulmonary embolism are also increasing because of an increase in western lifestyle. Since pulmonary embolism is often a fatal complication, it should be prevented by adequate knowledge and careful management.

Key words: Total hip arthroplasty; Complication; Dislocation; Infection; Pulmonary embolism

Introduction

The current method of total hip arthroplasty (THA) was first reported in 1961 by Charnley in England.[1)] During the 38 years that have passed since then, the painful condition of the hip joint, particularly in adult patients, has been treated with excellent functional performance. THA has achieved highly satisfactory results for both patients and surgeons. In Japan, there are about 40,000 hip replacement surgeries each year, combining THA and hemiarthroplasty. THA has a characteristic set of complications, which require careful management and prevention.

The six major complications of THA include 1) postoperative dislocation, 2) fracture, 3) infection, 4) heterotopic ossification, 5) aseptic loosening, and 6) venous thrombosis and/or pulmonary embolism. In this article, these complications are described along with their management and prevention.

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The Japanese text is a transcript of a lecture originally aired on October 29, 1999, by the Nihon Shortwave Broadcasting Co., Ltd., in its regular program “Special Course in Medicine”.

Fig. 1 Postoperative dislocation

A 78-year-old woman underwent THA for a fracture of the right femoral neck. Two months later, she fell at home and sustained postoperative dislocation, which was manually reduced under intravenous anesthesia on the same day.

Dislocation after THA

The incidence of dislocation after THA is 1–3%. It often occurs in the presence of soft tissue weakness and happens early after the operation before healing of capsular damage is completed.[2,3] Among such dislocations, 70% of the cases occur by one month after THA.

Postoperative dislocation after THA often occurs because of incorrect placement of the prosthetic components, particularly when anteversion of the socket is insufficient, or because the patient is confused or demented. The adequate angle of the socket which should be set is quite limited, i.e., it must be placed at an adduction angle of 40 ± 10 degrees and at an anteversion of 15 ± 10 degrees. Deviation from this range can allow the socket to impinge on the femoral head, leading to dislocation when the joint is flexed markedly or is flexed with adduction and internal rotation. Elderly patients often show mental deterioration that makes them incapable of avoiding dislocation by keeping the affected lower extremity in the proper position (Fig. 1).

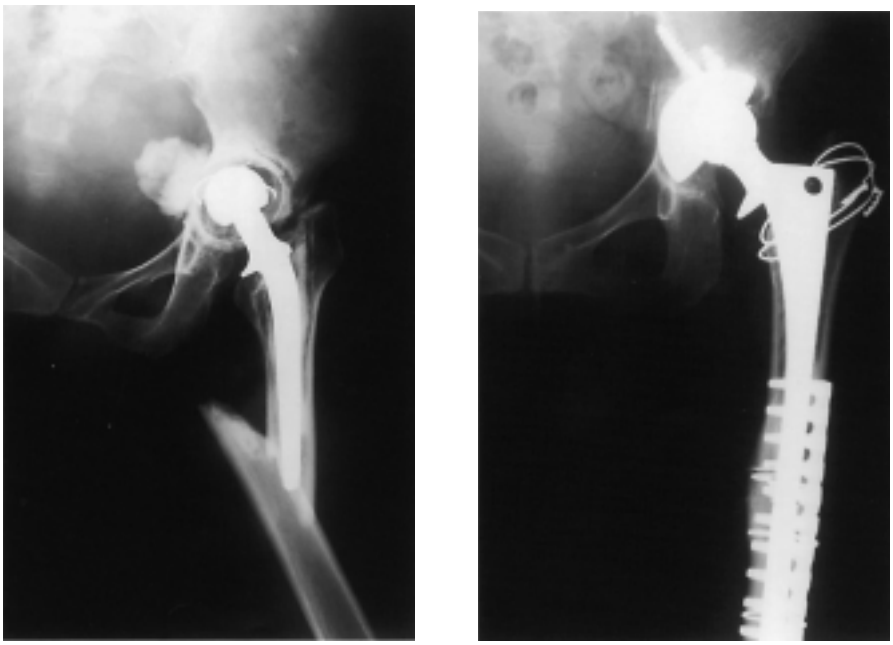
To prevent dislocation after THA, the surgeon should be sufficiently skilled in placing the prosthetic components properly. In addition, the surgeon must exercise caution because specific problems with the components may occur depending on the approach used and the patient's position. When the patient is placed in the lateral decubitus position during THA procedure, for example, the socket is prone to tilt backward. To keep it in the proper position, it must be remembered to adequately tilt it forward.

Selection of the correct prosthesis is also important. Implants with a head of 22 mm in diameter, for example, lead to a high risk of dislocation. In elderly patients who have a higher risk of dislocation, a prosthesis with a relatively large head seems to be the best choice. To prevent mental deterioration, it is also important to mobilize the patient from bed as early as possible.

If posterior dislocation occurs, which is the most common type, the affected lower extremity is shortened along with adduction and internal rotation. When such changes are noted, a diagnosis of dislocation must be confirmed by radiography, along with determination of the presence or absence of fracture. Without fracture, the dislocation is reduced manually as soon as possible under general or spinal anesthesia and the joint is immobilized in a spica cast for 3 weeks. If manual reduction is unsuccessful, open reduction will be necessary.

Fracture

Fractures can be classified into two categories depending on the time of occurrence. Those are intraoperative and postoperative fracture. Intraoperative fracture is often associated with the insertion of uncemented component. In this context, it should be noted that the use of uncemented prostheses has been



a b

Fig. 2 Fracture of the femoral shaft after THA

A 55-year-old woman underwent THA for osteoarthritis of both hips.

a. She sustained a fracture of the femoral shaft when she fell after THA. Because of the presence of a circumferential radiolucent line between the cement and bone around both of the two components (socket and stem), a diagnosis of bi-component aseptic loosening was made.

b. A radiograph taken two years after uncemented revision arthroplasty and stabilization of the fractured femoral shaft with a Mennen plate. Union of the femoral shaft is complete and there is firm fixation of the components implanted at revision surgery.

increasing recently.

In uncemented THA, as large a component as possible should be inserted into the medullary canal of the femur or into the acetabulum. The principle is that an uncemented component should be press-fitted into the bone, but this method makes the bone more vulnerable to fracture. In particular, in elderly or severely osteoporotic patients, great care must be taken not to cause fracture during surgery. If the femur is merely cracked without separation of the fragments, it can be easily repaired with cerclage wires around the femoral neck. In general, it is important for the surgeon to understand the characteristics of each prosthesis and to have sufficient skill.

Trauma such as a fall or a traffic accident can cause postoperative fracture, and it is difficult to treat such a fracture because of the existence of the prosthetic stem. If the prosthesis is loosened, it must be replaced by performing revision arthroplasty. If it is not loosened, open reduction and fixation with a plate are indicated (Fig. 2).

Even experts consider that fractures which occur after THA are difficult to treat and no systematic approach has yet been established. Before treating such fractures, consultation with experts is desirable.

Infection

Infections associated with THA can be classified into two major types, which are early infections occurring within 3 months after THA and late infections occurring from 3 months onwards. Superficial or deep infection occurs in about 1% of patients. The chief caus-

ative organism has been reported Staphylococcus epidermidis, followed by *S. aureus*.[4] Infection has traditionally been the most fearful complication of THA, and its prevention is extremely important.

The lower extremity must be washed before THA to make it as clean as possible, followed by careful antisepsis of the skin, the use of a clean operating room, removal of expired air by the operators wearing special suits like those for astronauts, and prophylactic use of antibiotics after surgery. After THA, blood tests such as measurement of C reactive protein (CRP) and the erythrocyte sedimentation rate should be performed regularly, along with examination of the temperature profile and the wound. When deep infection is suspected because of the persistence of postoperative fever, puncture of the hip must be performed without hesitation and the aspirate must be cultured to facilitate early diagnosis and early treatment.

Late infection can occur up to several years after THA. It may be due to organisms transmitted through the bloodstream from tonsillitis or other sources that colonize the prosthesis in some cases. To prevent late infection, we give patients a leaflet with instructions to be followed after THA. If infection occurs at a site other than the hip, the patient should be treated as soon as possible.

When deep infection has unfortunately developed, treatment becomes very complicated and difficult. Identification of the causative microbial agent is necessary, followed by administration of antibiotics, removal of the infected components, irrigation of the infected site, insertion of bone cement beads impregnated with antibiotics, and finally reinsertion of new components.

Revision arthroplasty can be performed in one or two stages. Various techniques have been proposed, depending on the causative agent and the severity of infection. Because choosing an appropriate therapeutic plan is quite complicated, as described above, consultation with specialists is desirable when infection of prosthetic hip components is diagnosed or suspected.

Fig. 3 Heterotopic ossification

A 47-year-old woman at 1 year after THA shows Grade 3 heterotopic ossification according to the Brooker classification (arrow). The range of motion is substantially restricted to 40 degrees of flexion, 15 degrees of abduction, 10 degrees of external rotation, and 10 degrees of internal rotation.

Heterotopic Ossification

The incidence of heterotopic ossification after THA has been reported to be about 20%. Although it has been believed to be higher in Westerners than in Japanese, it seems to be increasing among Japanese patients because of the wider use of uncemented components for THA (Fig. 3).

Severe heterotopic ossification, which restricts the range of motion according to the Brooker classification,[5] seldom occurs. Although the definite cause of heterotopic ossification is unclear, spreading of bone debris throughout the surgical field is considered to be one factor. Therefore, such debris should be removed completely by irrigation of the wound before closure.

When the occurrence of heterotopic ossification is more likely, as in patients who have severe osteoarthritis of the hip associated with marked osteophyte formation, prophylactic administration of indomethacin or other nonsteroidal anti-inflammatory drugs and X-ray irradiation can be effective. If heterotopic ossification restricts the range of motion, surgery to remove the bone masses is necessary.

Aseptic Loosening

Aseptic loosening is the most serious late complication of THA. It is an event that corresponds to the death of the prosthesis. "Loosening" is generally defined as progressive migration of a prosthetic implant over time, which can be demonstrated by repeated radiographic studies, or as the appearance of a circumferential radiolucent line with a width of 2 mm or more that surrounds the cement or a component on an X-ray film (Fig. 2).[6]

There are many factors that are considered to be responsible for the development of aseptic loosening. Typical factors include, 1) the surgical technique, 2) the design, materials, structure, and articulating surfaces of the prosthesis, and 3) patient factors such as the underlying disease, age, sex, weight, and level of activity.

In order to prevent aseptic loosening and prolong the life of the prosthesis, the surgeon should be skilled at performing THA and at choosing the appropriate implant. In addition, the patient should receive postoperative instructions that maintain as good a quality of life as possible. Because THA should be an operation that results in the patient walking well, we usually recommend that patients walk and travel as much as possible instead of instructing them to refrain from various activities.

If aseptic loosening occurs, it should be managed by revision arthroplasty to replace the loosened component. Once a component has become loose, the bone around it is destroyed progressively. Consequently, it is desirable to perform revision arthroplasty before the bone loss becomes excessive. In addition, revision arthroplasty takes longer and causes more bleeding than the primary THA, so it is harder for both the surgeon and the patient. Because the procedure is complicated and more often associated with problems such as fracture, it should be done by orthopedic surgeons who are skilled at performing THA.

Venous Thrombosis and Pulmonary Embolism

Venous thrombosis and pulmonary embolism are a current topic of interest. Traditionally, these complications have been considered to be uncommon among Asians, including Japanese. However, the incidence among Japanese patients has been increasing recently, possibly because of Westernization of the diet. Because perioperative death of some Japanese patients due to pulmonary embolism has been reported, these complications are now considered to be important.[7,8] In a recent prospective study, venography demonstrated venous thrombi in about 30% of Japanese patients undergoing THA.[9] Older age, female sex, and obesity are pointed out to be risk factors for venous thrombosis.

If deep vein thrombosis develops, it obstructs the venous return and causes the affected extremity to swell. If a thrombus is detached and carried by the blood, it may become trapped in the pulmonary artery. This causes a condition called pulmonary embolism, which is often fatal. Consequently, these two conditions seem to be sequential complications. Both are most likely to develop within 2 or 3 weeks after THA. Pulmonary embolism should be suspected if a patient complains of sudden chest pain and dyspnea after THA. It can be diagnosed by pulmonary angiography or by lung perfusion scintigraphy. Pulmonary embolism must be recognised as a potentially

fatal complication and preparation for its management is necessary. Pulmonary embolism can also be caused by fatty tissue from the medullary cavity that enters the bloodstream during the insertion of a prosthetic component and is carried to the pulmonary artery. When performing cemented THA, the medullary cavity should be debrided and cleaned thoroughly before the injection of cement.

As a preventive measure for pulmonary embolism, anticoagulants are used in Europe and in the United States. In Japanese patients, however, the use of anticoagulants makes it difficult to control bleeding and seems to be unsuitable. We usually use elastic stockings, and an instrument called the AV impulse after THA. This is a device that compresses the veins of the sole intermittently. If venous thrombosis occurs, thrombolytic therapy is given.

As described above, there are a number of important complications of THA. Because so many THA operations are performed these days, the operation should be planned in detail beforehand with the occurrence of these complications being taken into consideration. Care must be taken so that the development of complications can be prevented. After surgery, the temperature profile and the results of blood tests must be examined carefully, with careful maintenance of the operated limb in the proper position, in order to avoid complications such as infection and dislocation.

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Chronobiology in Dysautonomia and Cerebrovascular Disease

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Abstract: The study of chronobiology is based on the concept that homeostasis in the milieux interieur fluctuates within specific time cycles. Time-series data collected with a specific time frame are required to evaluate the characteristics of biological rhythms. Although no completely adequate method for the analysis of time-series measurements has been established, the new MemCalc system may be highly valuable. This system is very helpful to study biological rhythms that are difficult to elucidate using conventional analytical methods. It is ideal to perform infinite time-series analyses over continuing time, but current technology has its limitations. In this study, we reviewed disrupted biological rhythms in patients with dysautonomia or cerebrovascular disease within specific time frames of milliseconds, seconds, hours, days or still longer periods, focusing on time-series analyses of heart rate/blood pressure rhythm variations using the MemCalc system. We also introduced current chronological research findings relevant to this study. A chronobiological approach to heart rate/blood pressure rhythm variations using time-series analysis will enable clinicians to predict the occurrence and prognosis of cerebrovascular events or brain attack.

Key words: Heart rate/blood pressure variability; Time series analysis; Cerebrovascular disease; Neurodegenerative disease

Introduction

The concept of biological rhythms is based on temporal ordering. In this paper, we reviewed disrupted biological rhythms in neurologic disease within several specific time frames, focusing on a time-series analysis of heart rate/blood pressure variability, which has been widely employed in the clinical setting.

Blood Pressure Rhythm in Milliseconds

Various biological rhythms are noted in the living body in a continuous time cycle. In the case of the biological rhythm of blood pressure, a biological signal, the arterial pressure pulse wave is the smallest time rhythm that can be analyzed. Arterial pressure pulse wave analysis has been demonstrated to reveal the

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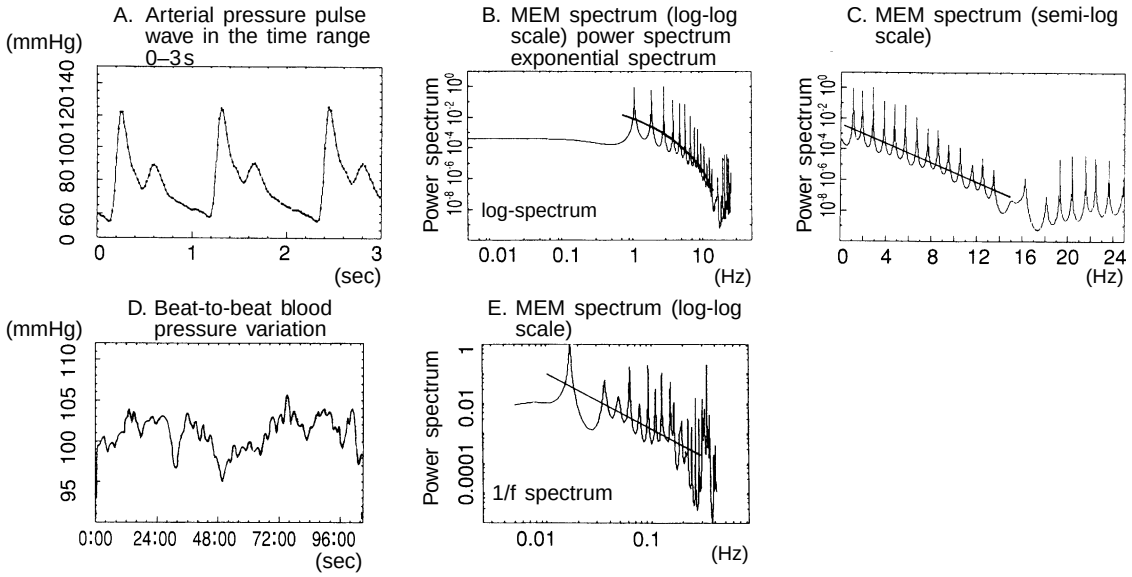

Fig. 1 Arterial pressure pulse wave and biological rhythms of beat-to-beat blood pressure variation

Upper panels: A. The arterial pressure pulse wave measured at the radial artery by tonometry in a 31-year-old healthy subject. B. MEM spectrum of the arterial pressure pulse wave illustrated in a log-log scale. The spectrum in the range of 1–10 Hz shows exponential characteristics and attenuation. C. MEM spectrum of the same arterial pressure pulse wave illustrated in a semi-log scale. The attenuation of the spectrum is linear and its gradient, the exponential coefficient, is -0.2719.
Bottom panels: Beat-to-beat blood pressure rhythm variation data obtained from the same healthy subject. D. Trend analysis of beat-to-beat blood pressure rhythm patterns from the radial artery for 100 s. E. MEM spectrum of the beat-to-beat blood pressure rhythm variation illustrated in a log-log scale; a 1/f spectrum attenuation is noted. The beat-to-beat variation shows a 1/f rhythm.

basic characteristics innate in biological rhythms, in contrast to the other time-frame analyses described below. Ohtomo *et al.* reported exponential spectral characteristics in the Lorenz/Roussler/Daffing model, known as the chaos dynamic system.[1] Ohtomo's study revealed for the first time in the world that chaos exists in biological time series, by proving that arterial pressure pulse waves have exponential spectral characteristics.[2]

Figure 1 shows the exponential characteristics of an arterial pressure pulse wave in a healthy subject. Unlike those of the 1/f spectrum described later, these exponential spectral characteristics do not vary between healthy people and patients with cerebrovascular disease or neurodegenerative disease associated with dysautonomia. Thus, these exponential spectral characteristics may be essential to biological activities.[3] The coefficient of the exponential characteristics, however, has been reported to be affected by mental stress.[4]

Note 1) Maximum entropy method (MEM): MEM is a spectral analysis method proposed by Jaynes, based on the concept of informational entropy. MEM analysis, which has been widely used, applies an algorithm suggested by Burg. MEM rapidly estimates the spectrum of the observation data with high resolution.

Note 2) MemCalc system: MEM analysis has the problem of lag dependency in power spectral density (PSD). Ohtomo, Tanaka and coworkers[13] resolved this problem in determining the optimal lag in such a way as not to be in conflict with the MEM theory, based on the analysis of the sunspot. This has been proposed as the MemCalc system. The system is a time-series analytical method, which combines the MEM spectral analysis method and the nonlinear least squares method (LSM). Since least squares fitting calculated by the LSM reproduces the original time-series data, the validity of the MEM spectrum can be confirmed.

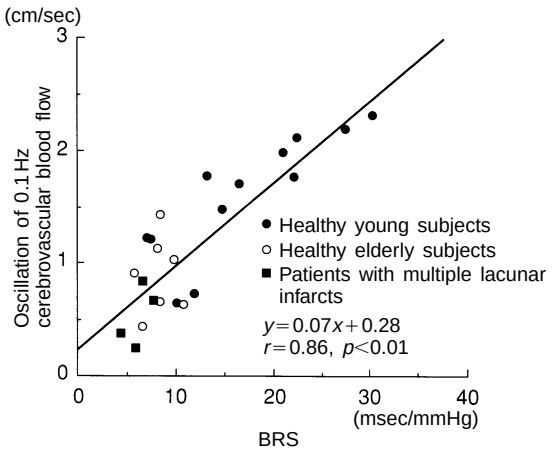

Fig. 2 Relationship between 0.1 Hz-cerebrovascular blood flow rhythm and baroreceptor sensitivity

In this plot, the y axis describes the oscillation of the 0.1 Hz-cerebrovascular blood flow rhythm, obtained by spectral analysis using the MemCalc system for the blood flow velocity at the middle cerebral artery, which was measured by transcranial Doppler ultrasound; the x axis illustrates baroreceptor sensitivity based on the ratio of heart rate and blood pressure rhythms of around 0.1 Hz. The lower the BRS, the smaller the oscillation of the 0.1 Hz-cerebrovascular blood flow rhythm. The two parameters are lower in healthy elderly subjects ($n=7$) than in healthy young subjects ($n=12$). Both parameters are the lowest in patients with multiple lacunar infarcts associated with leukoaraiosis ($n=4$), indicating that the 0.1 Hz-cerebrovascular blood flow rhythm is related to the risk of cerebrovascular infarction and the BRS.

Heart Rate/Blood Pressure Rhythms in Seconds

Heart rate/blood pressure rhythms on a time cycle of seconds are directly related to autonomic activity and are measured in many clinical situations for evaluating autonomic function via the baroreceptor reflex. Blood pressure rhythms of around 0.1 Hz (10-second cycles) and heart rate rhythms of around 0.25 Hz (4-second cycles) are known to reflect vasomotor sympathetic activity and vagal activity, respectively, while the ratio of the heart rate and blood pressure rhythms, each around 0.1 Hz, is known to reflect the vasopressor reflex function. These biological rhythms are disturbed in patients with neurodegenerative disorders associated with dysautonomia, such as in Parkinson's disease, multiple system atrophy, pure progressive autonomic failure,[5] and cerebrovascular disease. The severity of autonomic dysfunction can be assessed according to variations in these heart rate/blood pressure rhythms.

Furthermore, biological rhythms in seconds have been detected not only in the heart rate and blood pressure, but also in respiration, muscle nerve sympathetic activity,[6] electroencephalographic activity and cerebral blood flow. In time, a possible correlation between these various biological rhythms in our body may be elucidated as shown in Fig. 2. A rhythm of around 0.1 Hz has been recognized in blood flow to the brain as in the blood pressure, but this rhythm is considered to be under a different regulatory mechanism to that of the blood pressure rhythm. The rhythm in cerebral blood flow is attenuated in patients with multiple lacunar infarcts associated with leukoaraiosis.[7] Such attenuation is closely related to blunted baroreceptor reflex function, suggesting that cerebral arteriolosclerosis may affect the mechanism regulating the rhythm.

On the other hand, Kobayashi and Musha have demonstrated that the arterial pulse pressure wave and beat-to-beat blood pressure rhythm variations exhibit a 1/f spectrum, as shown in Fig. 1.[8] The $1/f^{\beta}$ spectrum has been identified as an intermittent chaotic phenomenon, which also indicates that the regulatory mechanism of these heart rate/blood pressure rhythms is closely related to autonomic function. Ohtsuka *et al.* have clarified that the slope of 1/f, or the elevation of β, is affected by atropine loading, aging, and Parkinson's disease.[9]

Blood Pressure Rhythms in Hours (Mainly Circadian Rhythms)

Twenty-four hour time-series data of heart rate/blood pressure can be readily collected by Holter recording and ambulatory blood pressure monitoring. Abnormal circadian rhythms have been observed in many disease conditions. Recognition of impaired circadian

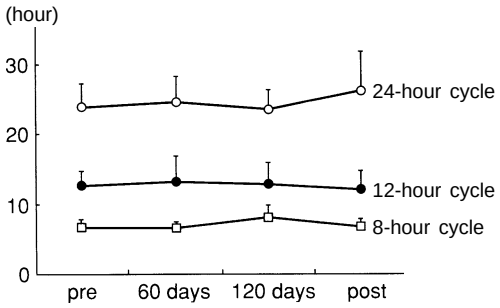

Fig. 3 Twenty-four hour systolic blood pressure rhythm variations in a 120-day 6° head-down bed rest study (unpublished data)

Twenty-four hour blood pressure rhythm variations can be measured in basic cycles of 8, 12 and 24 hours. Blood pressure measurements in such cycles were performed to compare the values obtained at baseline, after 60 days of bed rest, after 120 days of bed rest, and at the end of the experimental period, and were analyzed using the MemCalc system. The bed rest study allowed the subjects to be physically inactive and under microgravity. However, no changes were observed in the structure of the systolic blood pressure rhythms in these basic cycles.

rhythms is essential to chronobiological treatment.

Blood pressure during sleep is usually 15 to 20% lower as compared with that during physical activity. Subjects showing such physiological nocturnal decline are referred to as dippers. Patients with hypertensive or cerebrovascular disease often do not show the physiological nocturnal decline in blood pressure and are referred to as non-dippers. However, some hypertensive patients are extreme-dippers, and show a nocturnal blood pressure decline of more than 20% as compared to the daytime blood pressure.[10] Non-dipper or extreme-dipper patterns of nocturnal blood pressure decline in patients with hypertension are more likely to be associated with target organ damage. The incidence of cerebral infarction has been reported to be significantly high in association with these patterns.[10]

Since it has been suggested that the chance of occurrence of cerebral infarction is at its highest in the early morning, the finding of the morning surge in blood pressure in association with a disrupted circadian rhythm has drawn many researchers' attention. For the prevention of cerebrovascular attacks, control of such impaired circadian patterns of blood pressure, especially such as the morning surge or non-dipping patterns of blood pressure in hypertensive patients, has therefore been emphasized, and α_1 blockers have been successfully used in the management of excessive blood pressure surges in the early morning.[10]

The circadian rhythm of blood pressure could be influenced by exogenous factors. The two strongest modifiers are believed to be physical activity during sleep and wakeful stages, and mental stress. Neurologic disease is generally associated with motor dysfunction. Reduced physical activity associated with motor dysfunction has also been considered to contribute to the disrupted circadian rhythm of blood pressure in patients with cerebrovascular diseases or Parkinson's disease.

Figure 3 shows the circadian rhythms of blood pressure obtained from a 6° head-down bed rest study. Bed rest study is an approach used in space medicine, in which subjects are immobilized at bed rest in a supine position in microgravity for 24 hours. The protocol of a 120-day bed rest study was accepted by the ethical committee of the State Scientific Center Institute of Biomedical Problems in Russia, and all the 6 healthy male volunteers gave informed consent.

In this study, the circadian rhythm of blood pressure was measured in basic 8-, 12- and 24-hour cycles to compare the values obtained at baseline, after 60 days of bed rest, after 120 days of bed rest, and at the end of the study. No significant changes in these basic cycles of circadian rhythms were observed at these time points. These findings indicated that physical inactivity during sleep or wakefulness has no effect on the circadian rhythms of blood pressure. Therefore, disrupted circadian rhythms of blood pressure in patients with neurologic disease may result from the disease itself.

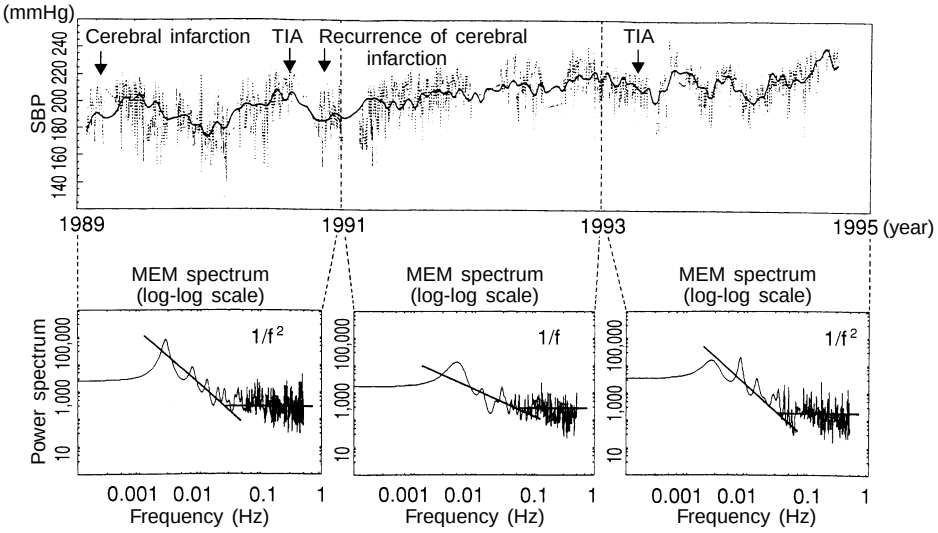

Fig. 4 Changes in systolic blood pressure (SBP) rhythms over 6 years in a patient (from 71 to 77 years old) with cerebral infarction associated with complete occlusion of the right internal carotid artery

Blood pressure was measured daily with a home sphygmomanometer at a prescribed waking time in the morning. The data for every 2 years were analyzed using the MemCalc system. The upper panel shows trend analysis of the SBP and the bottom panels represent the corresponding MEM spectrum illustrated in a log-log scale. The MEM spectrum showed a $1/f^2$ rhythm from 1989 to 1991, interposed by two cerebral infarction events and one transient ischemic attack (TIA). A $1/f$ rhythm was observed from 1991 to 1993, and the $1/f^2$ rhythm was again noted from 1993 to 1995.

Blood Pressure Rhythms in Periodic Cycles of Days or Longer

Brain attacks, including cerebral infarction, have been reported to be more common on Mondays and during winter.[11] These findings suggest that weekly or yearly circadian patterns may influence the risk of cerebrovascular events. Blood pressure rhythms in 7-day cycles have been reported.[11]

Few studies on blood pressure rhythms in cycles of 7 days or longer have been reported. We conducted blood pressure measurements over 2 years in patients with cerebral infarction or Parkinson's disease, using a home sphygmomanometer. The collected data were analyzed by the maximum entropy method (MEM).[3,12]

The results showed that the incidence of cerebral infarction shows a yearly cycle, with a peak during the winter season. The MEM spectrum showed a $1/f^2$ rhythm in 6 out of 10 patients with cerebral infarction and a $1/f^0$ rhythm in 2 out of 3 patients with Parkinson's disease, while a $1/f$ rhythm was observed in 7 out of 10 healthy controls. The $1/f^2$ rhythm, known as brown noise, is strongly confined to past time series and is less flexible to the body. $1/f^0$, or white noise, is characterized by random fluctuation.

Figure 4 shows the results of MEM spectral analysis of daily blood pressure data measured over a period of 6 years in a patient with cerebral infarction. The blood pressure rhythms varied even within the same patient over specific time periods. The data also indicate that the onset of cerebrovascular events may be associated with a month or longer of disrupted blood pressure rhythms.

Conclusion

More and more genetic research for understanding biological rhythms has been per-

formed since the clock genes were identified in humans. The role of the nervous system network is practically important for understanding the biological rhythms of the body. On the other hand, analysis of biological rhythms, such as that of the heart rate or blood pressure, both of which are target parameters in the study of the control or maintenance of physiological function, provides an overall approach in terms of the self-organized systematization of these parameters. Further studies taking these two viewpoints into consideration are warranted to understand biological rhythms in greater detail.

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Lifestyle is Not the Only Cause of Stroke —Risk Factors Recently Attracting Attention—

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Abstract: Cerebrovascular disease (stroke) remains the most common disease in Japan and other Asian countries despite the decrease in stroke mortality. It was expected that the incidence of stroke would decrease in line with the mortality rate, but it has not. The major causes of stroke include hypertension, diabetes, and hyperlipidemia, while alcohol, smoking, obesity, hyperuricemia, and polycythemia are other risk factors. All of these factors are closely related to lifestyle. In some cases, however, factors unrelated to lifestyle or generally ignored to date are involved in the etiology of stroke, particularly in young adults. Lipoprotein(a), C-reactive protein, infection with Chlamydia pneumoniae, anti-phospholipid antibodies, and genetic factors are typical risk factors for stroke that are not related to lifestyle. Homocysteine and hyperinsulinemia are also risk factors for stroke, although they are related to lifestyle to some extent. In this article, risk factors for stroke other than the conventional lifestyle-related factors are discussed briefly, mainly based on data obtained from patients whom we have examined. Our findings have emphasized that when risk factors unrelated to lifestyle are combined with lifestyle-related factors, there is a syngeristic effect on the development of stroke.

Key words: Risk factors for cerebral infarction; Stroke in young adult; Lifestyle-related disorder; Stroke and genetics

Introduction

Cerebrovascular disease (stroke), along with heart disease, remains the second or the third leading cause of death after malignancy despite the recent remarkable decrease in mortality. Moreover, the proportion of patients treated for stroke, as well as the prevalence of stroke, has remained unchanged or even tended to increase.

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In Japan, despite the decrease in mortality, the incidence of stroke has not yet decreased so much, so stroke remains a typical national disease. Indeed, it seems to be a great achievement of preventive medicine that stroke is becoming milder than before. Because there is still no effective therapy for a completed stroke, however, prevention of stroke or control of risk factors is very important.

Do All Strokes Stem from Lifestyle?

Hypertension, diabetes, and hyperlipidemia are the well-known major causes of stroke. There is no doubt that all these conditions, as well as drinking, smoking cigarettes, obesity, hyperuricemia, and polycythemia, are risk factors closely related to lifestyle. An individual's lifestyle seems to influence even multiple risk factor syndrome (synonymous with syndrome X or the deadly quartet), which is a risk factor for atherosclerosis and a current focus of attention. Overnutrition and stress are thought to play a role in the accumulation of fat in various organs, producing the basis for pathological changes of the atherosclerosis.

However, stroke is not necessarily a lifestyle-related disease in all cases. There is even a possibility that causes unrelated to lifestyle will become more predominant if our lifestyle is modified in the future. Not only do strokes develop in the elderly, but also in relatively younger adults aged 45 or below. In a survey that we performed several years ago,[1] younger adults accounted for about 25% of patients with cerebral infarction. Stroke in younger adult arose from risk factors closely related to lifestyle in only about one fourth of them, but the causes were unrelated to lifestyle in the remaining three fourths. Even among patients older than 45 years, the primary cause was not one of the well-known risk factors in about one third of them.

Among the risk factors for ischemic cerebrovascular disease, those not directly related to lifestyle will be discussed briefly in this article.

When Should Special Risk Factors Be Considered?

Uncommon risk factors should be considered in stroke patients particularly under the following conditions: 1) relatively young patients (aged 45 or less), 2) the absence of any common risk factors such as hypertension, diabetes, or hyperlipidemia, 3) a family history of frequent recurrent stroke, 4) frequent recurrence of strokes over a short period, and 5) coexisting symptoms of dementia, collagen disease, or severe or frequent headache.

Risk Factors to Be Considered

(1) **Lipoprotein (a)**

The first risk factor to be discussed is lipoprotein (a), which has attracted attention recently. Lipoprotein (a) (Lp (a)) is an LDL-like lipoprotein that has gained attention as a substance which may link thrombus formation and atherosclerosis. According to a study performed at my department, the plasma Lp (a) level is normally 10–20 mg / dL or less, but the mean level is as high as 28 ± 20 mg / dL in atherothrombotic cerebral infarction, and is particularly high in younger adults with stroke.[2]

Each person has a rather constant level of plasma Lp (a) that remains unchanged throughout life, except during childhood, and this level is defined by autosomal dominant inheritance. Independence of diet and other lifestyle factors characterises Lp (a). Because about half of the individuals with high plasma levels of Lp (a) have no other risk factor for cerebral infarction, it can be considered as a single genetic risk factor for stroke. The plasma level can be measured easily, so Lp (a) is one factor to be assessed in patients with cerebral infarction.

(2) **Homocystine**

A disease called homocystinuria is known

as one of the congenital aminoacidopathies. It is characterised by mental retardation, seizures, lens subluxation, and spider-like fingers. It is a very rare disease, but is known to be associated with a propensity for generalized arterial and venous thrombus formation. We have previously reported a patient with this disease.[3] It has also become known, however, that the plasma homocystine concentration is often elevated without manifestation of any of the above symptoms. In the United States, Boushey *et al.* performed a meta-analysis of 27 reports on the association between plasma homocystine levels and vascular disease. They reported that the incidence of cerebrovascular disease increased by 1.5 times when the plasma homocystine level increased by 5μmol/L.[4] At the conference of the Japanese Society of Stroke, for which I was the President, in April 1999, Professor Toole from the United States gave a special lecture. He also emphasized the association between elevation of the plasma level of homocystine and ischemic cerebrovascular disease.[5]

In the United States, a large-scale study is underway on homocystine as a risk factor for cerebrovascular disease, but little investigation has been performed in Japan. My group has some data, but there is still not enough information. Because homocystine can be measured easily, however, it should also be determined in cerebral infarction patients if the cause is unknown. In addition, the homocystine level is known to rise if the dietary intake of folic acid is inadequate. If data indicate that the homocystine level is increasing in Japanese subjects, the elevation could be attributed to lifestyle changes.

(3) **C-reactive protein**

It has long been suggested that inflammation may be involved in the pathogenesis of atherosclerosis. C-reactive protein (CRP), one of the markers of systemic inflammation, was monitored in 543 individuals for 8 years in a study performed by Physician's Health Study in the United States.[6] It was shown that CRP was significantly increased in individuals who developed myocardial infarction or cerebral infarction during the study period. It has also been reported that the outcome of cerebral infarction is poor if CRP is elevated at the onset.[7] Although the importance of CRP has been underrated in the past, it can be considered as a risk factor or as a predicting factor for stroke that is independent of lifestyle. However, it seems inappropriate to simply regard CRP itself as the only culprit in such patients.

(4) **Chlamydia pneumoniae infection**

There may be several microbial agents that cause infections related to stroke. Among them, Chlamydia pneumoniae infection has attracted attention recently. Chlamydia pneumoniae is a relatively new species of Chlamydiae that was established in 1989. It is found worldwide as a major causative agent of respiratory tract infections such as pneumonia, bronchitis, and pharyngitis. Antibodies have been reported to be positive in about 40–50% of adults in Europe and the United States. In Japan, the positive rate in the elderly seems to be as high as 70%.

Yamashita[8] has demonstrated immunoreactivity to Chlamydiae in more than half (55%) of the atherosclerotic lesions from patients with severe stenosis of the internal carotid arteries and has confirmed the presence of many Chlamydial elemental bodies in atheromatous plaques by electron microscopy. He also performed multivariate analysis and reported that Chlamydia pneumoniae infection is an independent risk factor for stroke. In Europe and the United States, it has been reported that antimicrobial agents such as azithromycin were effective in preventing the progression of atherosclerosis in patients with ischemic heart disease. More than one large-scale clinical study on this topic is still in progress.

(5) **Antiphospholipid antibodies**

It is widely known that patients with connective tissue diseases or so-called collagen

diseases are predisposed to cerebral infarction or cerebral venous thrombosis while they are young. In particular, systemic lupus erythematosus (SLE) is not only associated with cardiogenic cerebral infarction, but is also frequently associated with anti-phospholipid-antibody positive cerebral infarction. Furthermore, cerebral infarction with positive anti-phospholipid antibody not infrequently occurs in the absence of SLE. If anti-phospholipid antibodies such as anti-cardiolipin antibodies and lupus anticoagulant are measured particularly in female patients with frequent reoccurrence of cerebral infarction, it may be possible that their unknown cause of stroke becomes evident.

Data collected by my group showed that anti-phospholipid antibodies were positive in 8.8% out of 273 patients who had cerebral infarction without SLE, and more than one third of them had no other risk factors such as hypertension or diabetes.[9,10] Based on these results, anti-phospholipid antibodies were also concluded to be an independent risk factor for cerebral infarction. A follow-up study performed for an average of 7 years demonstrated that the recurrence and mortality rates were significantly higher among patients having high anti-phospholipid antibody titers. Abnormal activation of protein C is thought to be responsible for the development of cerebral infarction in patients with positive anti-phospholipid antibody.

(6) **Other coagulation disorders**

Not only the protein C abnormality described above, but also disorders of the coagulation and fibrinolysis system such as deficiency of protein S or antithrombin III, and congenital defects of plasminogen, may cause cerebral infarction, particularly in young persons. One of these components of the coagulation and fibrinolysis system was abnormal in as many as 28 out of 77 cerebral infarction in younger adult that we studied.[11] Consequently, these risk factors should be assessed in cerebral infarction of unknown cause in younger adult. The details will be described elsewhere because space is limited. As coagulation disorders caused by abnormalities such as those described above are only transient in some cases of cerebral infarction in younger adult, however, I would like to emphasize the need to start evaluating for these factors in the acute phase and to repeat the investigations at intervals.

Are Genetic Factors Involved in Stroke?

As the last subject, I would like to discuss the genetic aspects of cerebral infarction briefly, although this is not directly related to lifestyle. The familial occurrence of cerebral aneurysm, which is the major cause of subarachnoid haemorrhage, is well known. In addition, Sekiyama in my department has reported the possibility that the ApoE4 gene is involved in the development of atheromatous lesions in the carotid arteries and other major arteries.[12] Moreover, Tachikawa in my department has demonstrated that the mutant α-1-antichymotrypsin 1 gene, which we found several years ago,[13] is strongly involved in ischemic cerebrovascular disease, particularly lacunar infarction.[14] Furthermore, Kario *et al.* reported that the gene for angiotensin-converting enzyme is involved in ischemic cerebrovascular disease secondary to hypertension.[15] In the near future, as a consequence of progress in genetic studies, the genetic aspects of this disease will be further elucidated.

Conclusion

Even apart from genetic aspect, the evaluation of risk factors not directly related to lifestyle should be also conducted thoroughly, particularly in younger patients with cerebral infarction. Some of the causative disorders are treatable, if they are detected before stroke occurs. Detection of these factors is important

for both physicians and patients from the viewpoint of primary and secondary prevention of stroke.

Finally, I would like to emphasize that lifestyle modification should not be disregarded, because even risk factors unrelated to lifestyle seem likely to potentiate the role of conventional risk factors in the development of stroke. Furthermore, even if conventional risk factors are predominant, the concurrent involvement of other factors should be considered, if necessary.

Because space was so limited, the risk factors for cerebral haemorrhage could not be addressed in this paper and only some of the recently highlighted factors for cerebral infarction were discussed.

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Early Schizophrenia: A New Clinical Entity

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Abstract: Early schizophrenia as discussed in this paper is defined as "the early phase of a first-time *Schub* (acute exacerbation)" based on the definition of schizophrenia as "a chronic brain disease characterized by repetition of a specific *Schub* developing from the early phase to the full-blown phase and then to the sequela phase". In the past, this stage was called the prodromal phase because only nonspecific symptoms were generally observed. By referring to several prior references, the author re-discovered that symptoms specific to schizophrenia, although subtle, are latent in this stage. Considering the factors that the patient in this phase has an insight into his/her disease, typical antipsychotic agents such as chlorpromazine and haloperidol are not always effective, and patients often remain at this phase for several years, and hoping to increase early detection and early treatment of schizophrenia, the author proposed to describe this phase as early schizophrenia, a new clinical entity, in 1990. This paper re-iterates the concept of early schizophrenia and discusses the gender ratio, the age at onset, the clinical picture (diagnosis) and the treatment based on the author's clinical experience of more than 10 years.

Key words: Early schizophrenia; Schizophrenia; Prodrome; Early diagnosis; Early treatment

Introduction

The early stage of schizophrenia is, in quite general terms, referred to as early schizophrenia, but this paper discusses "early schizophrenia" proposed as a new clinical entity by the author based on the new definition in 1990.[4–10] The relation between early schizophrenia and ordinary schizophrenia may be likened to that of early cancer and advanced cancer. As the concept of early cancer prompted early discovery and early treatment of cancer, the main purpose of the author's proposed concept of early schizophrenia is to contribute to early discovery and early treatment of schizophrenia. The concept, the gender ratio, the age at onset, the clinical picture, and the treatment are discussed below.

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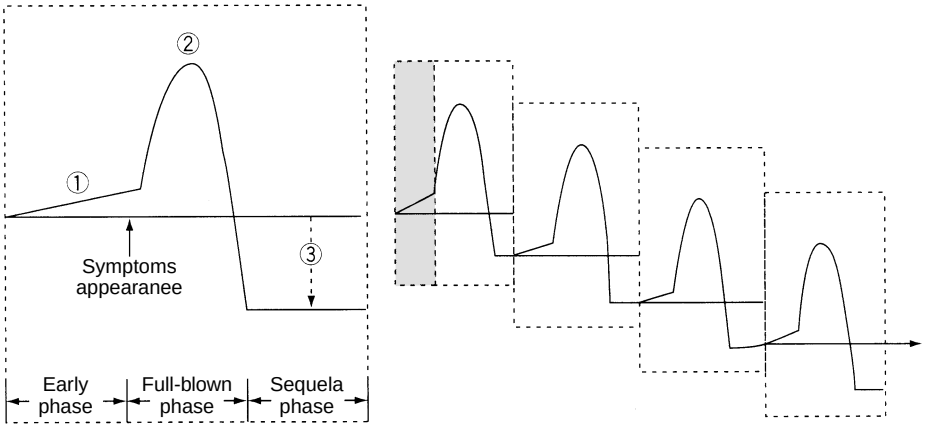
The Japanese text is a transcript of a lecture originally aired on May 2, 1999, by the Nihon Shortwave Broadcasting Co., Ltd., in its regular program "Special Course in Medicine".



① Early symptoms
Autochthonous experiences; heightened awareness; a vague sense of being watched; tense and perplexed mood

② Full-blown symptoms
Auditory hallucination; delusional perception; ego disturbance; catatonic syndrome

③ Sequela symptoms
Blunted effect; hypobulia; loosening of association

Fig. 1 Schematic representation of the progression and course of schizophrenic *Schub* and early schizophrenia

Left: The horizontal baseline indicates the state before each episode (or before the onset in the case of the first episode). The area above the baseline indicates the appearance of positive symptoms and that below the baseline the appearance of negative symptoms.

Right: The progression of schizophrenia is understood as continuation of individual episodes, and the baseline descends as the number of episodes increases. Early symptoms appear in each episode, but only the early phase of the first episode (gray area) is called early schizophrenia.

Concept

The definition of early schizophrenia[4] is based on the definition of schizophrenia (excluding hebephrenic schizophrenia) of "a chronic brain disease characterized by repetition of a specific *Schub*, developing from the early phase to the full-blown phase, and then to the sequela phase" and reads as "a clinical entity meaning the early phase of a first-time schizophrenic *Schub* and requiring a different treatment strategy than that for ordinary schizophrenia" (Fig. 1). It is pointed out, however, that this "early phase of a first-time *Schub*" means the stage, which used to be referred to as "the prodromal stage" prior to the onset. Generally, this stage used to be described as presenting symptoms non-specific to schizophrenia such as unidentified mental and physical complaints and neurotic symptoms.

As the author repeated careful examinations by referring to several prior studies,[1–3] it was noted that symptoms specific to, albeit subtle, schizophrenia were latent in the patient in this stage. In the beginning, there were observed four major symptoms or ten minor symptoms, which were described as "four major symptoms specific to early schizophrenia",[4, 6] and followed by observation of 30 specific and non-specific symptoms of early schizophrenia.[9] They will be discussed in further detail in the section of clinical picture.

The author has four reasons for treating early schizophrenia as a clinical entity different from ordinary schizophrenia; (1) symptoms specific to this phase are present, (2) patients in this phase have insight into or awareness of the disease unlike patients in the full-blown phase, (3) typical dopamine recep-

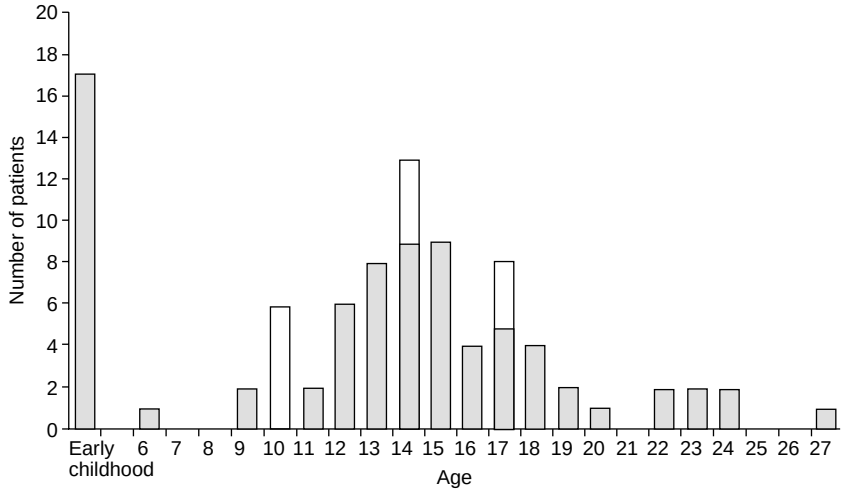


Fig. 2 Age at onset of early schizophrenia ($n = 90$)
Blank bars indicate the times at onset described vaguely (from left to right) as "in primary school", "in middle school", and "in high school" as the median age of each period.

tor blocking anti-psychotic agents such as chlorpromazine or haloperidol, which are effective for the full-blown phase, are not effective, suggesting that dopamine receptor blockers are not involved in its pathophysiology, and (4) patients often remain at this phase for an extended period of time without progressing to the full-blown phase (indicating the presence of a defense mechanism against progression to the full-blown phase.)

Gender and Age at Onset

As for the gender and the age at onset, both the author and his colleagues observed that the ratio was 1:1 for males and females as in ordinary schizophrenia, and the age distribution at onset had two peaks, early childhood and 14–15 (Fig. 2).[10]

Four-fifth of 90 cases were distributed in puberty, and the mean age among 73 patients that they personally examined was 15.0 ± 3.9. In one-fifth, some early symptoms had already appeared in early childhood, but exacerbation occurred in puberty. The mean age at which exacerbation occurred in these 17 cases was 15.6 ± 3.2, coinciding with that of the age at onset in puberty cases. The mean age at first examination was 18.9 ± 4.5, which was 3 to 4 years after the onset. This may be because symptoms are so subtle that both the patient and the family do not realize that they are caused by the disease.

Clinical Picture

As discussed above, there are as many as 30 symptoms observed in early schizophrenic patients if the specificity to schizophrenia is not questioned. In 102 cases examined by the author and his colleagues, prevalence of these symptoms of early schizophrenia was studied and 10 symptoms were frequently observed in more than 1/3 cases (33% or more), and these were classified into four higher rank groups (Table 1, Fig. 3).[9] It is almost impossible to check the presence/absence of 30 symptoms in a clinical setting, but it becomes comparatively easy if the symptoms are limited to 10 that are most frequently observed. They are considered useful for diagnosis because of their high frequency. These 10 frequently seen symptoms of early schizophrenia are briefly discussed.

1) Autochonous thinking is thoughts that come spontaneously to mind. For instance, a

Table 1 Highly Frequently Observed Symptoms of Early Schizophrenia Useful for Diagnosis

1. Autochthonous experiences
   - Autochthonous thinking
   - Autochthonous recollection
   - Autochthonous fantasy images
   - Autochthonous music images (musical hallucinations)

2. Heightened awareness
   - Heightened auditory awareness

3. Tense and perplexed mood and its related symptoms
   - Tense and perplexed mood
   - A vague sense of being watched and/or "Leibhaftige Bewußtheit"
   - Suspicion of being observed and commented on by the people around

4. Disorders of immediate cognition
   - Disorders of immediate understanding and judgment
   - Disorders of immediate memory

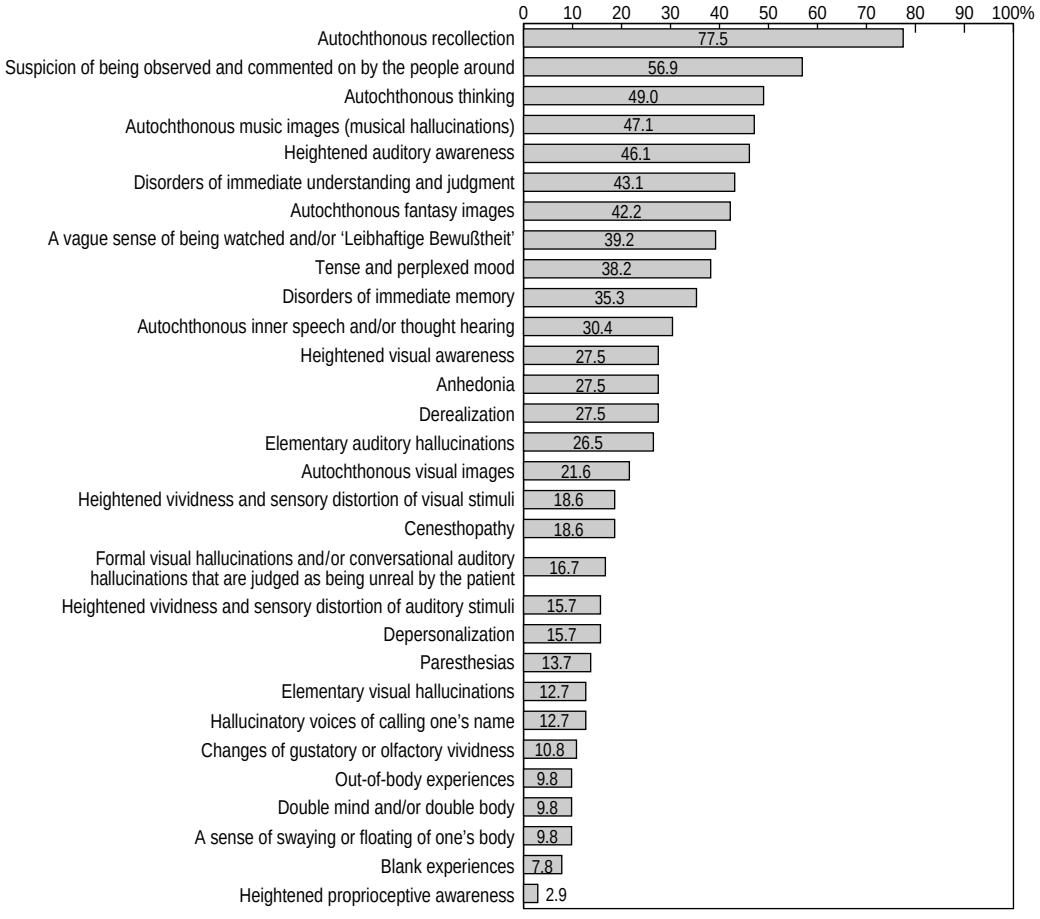


Fig. 3 Incidence of (30) symptoms of early schizophrenia ($n = 102$)

patient complains that "thoughts that are irrelevant to what I am consciously thinking come to me in surges". Rambling and incoherent thoughts come to the mind in succession.

2) Autochthonous recollection is experienced when "scenes of by-gone days come to mind frequently. They are usually scenes of myself playing with friends, clear and colorful as in the actual setting, and people move and the scene changes. I do not think I hear voices, but I feel as if I am conversing with someone" according to a patient. Emotional scenes that the patient experienced in the past spontaneously come back to him without relevance to the current situation or mood, and he can "see it inside his head or hear the sound actually".

3) Autochthonous fantasy images are explained by a patient as follows. "The name of someone I like comes to mind and I feel that the person is actually with me and I talk to that person. I am half aware that they are fantasies, but half the time I am totally immersed in that scene in the other half. When I come to myself, I find me sitting in front of the desk." This is generally described as daydreaming, and consists of visual and auditory images of a fantasy scene unfolded like a story.

4) Autochthonous music images are explained as follows. "I feel like I am giving a concert in my mind. Commercial songs and popular songs that I half know come and go in quick succession." The expression "autochthonous music images" is used to indicate that this is also an autochthonous experience, but it may be described as musical hallucination. Autochthonous thinking, autochthonous recollection, autochthonous fantasy images, and autochthonous music images as discussed above fall under a higher rank concept that is widely referred to as "autochthonous experiences".

5) Heightened auditory awareness is an experience such as "I become highly agitated when I suddenly hear other people's voices, sudden noises such as opening of the door or the sound of an electric train running nearby". A person becomes unintentionally aware of auditory stimulus of a slight sound or a human voice that suddenly and unexpectedly comes into his surroundings, and his attention is diverted by the sound. This is often accompanied by astonishment. Although the incidence of such phenomenon did not exceed 1/3 of the total, there are symptoms such as heightened visual awareness and heightened proprioceptive awareness that fall in the same category. This symptom should therefore be classified under the higher rank concept of "heightened awareness".

6) Tense and perplexed mood is described as "suppose I am up on stage. Before that, you get tense. I continually have that kind of feeling." While the patient is tense because he anticipates some incident, he is perplexed because he does not know what he is anticipating. This mood consist of autochthonous tenseness and perplexion.

7) A vague sense of being watched and/or "Leibhaftige Bewußtheit". For instance, a patient says "I am studying at night in my room and have the feeling that I'm being watched from behind by a spirit. When I turn around, no one is there, but when I look forward, I feel again that someone is still watching me." The sense of being watched is clear and certain, but the patient knows that there is actually nobody looking at him. As for this "watcher", there are various types ranging from vague and unclear (vague sense of being watched) to clear perception of the presence (Leibhaftige Bewußtheit).

8) Suspicion of being observed and commented on by the people around. A patient says that "when I see people talking around me, I feel that they are watching me or commenting about me, even though I half know that it is not so." In a place with people around, he feels that he is being watched or being commented on with malice. Different from delusion of persecution, he thinks only half of what he believes (or to be more pre-

cisely, believes it now and denies it the next moment).

The above discussed three symptoms, i.e., tense and perplexed mood, a vague sense of being watched and/or "Leibhaftige Bewußtheit" and suspicion of being observed and commented on by people around may be summarized as a higher rank concept of "the tense and perplexed mood and its related symptoms".

9) Disorder of immediate understanding or judgment. For instance, a patient feels that "it is hard to understand what others are talking or what is being said on television, and it is not possible to reconstruct the content in mind", "I am impatient because I lack judgment. For instance, chopsticks are standing in a chopstick stand, ... and I cannot immediately tell the differences". He is no longer able to understand the daily conversation of other people, which he used to understand instantly, or he cannot see the differences in shape or color as in the case of chopsticks discussed above.

10) Disorder of immediate memory. A patient working as a temporary help in a souvenir shop in an amusement park said, "I forget what I was going to do. Because I forget all the time so that when I am asked to go to the warehouse to fetch something, I always take a piece of the thing that I am supposed to fetch with me." The patient experiences that he cannot remember what he was going to do or what he was told immediately before. This disorder of immediate memory is not continuous as in the case of dementia, and is characterized by its random appearances.

These two types of disorders, i.e., disorders of immediate understanding and judgment and disorders of immediate memory may be summarized as a higher rank concept of "disorders of immediate cognition".

As discussed above, the 10 symptoms are frequently observed in more than 1/3 of early schizophrenia patients. According to the author's study of 102 cases,[9] the mean of symptoms was 4.7. In other words, all patients experienced approximately half of these symptoms (Fig. 4), demonstrating the author's theory that confirming the presence of these symptoms is useful for diagnosis.

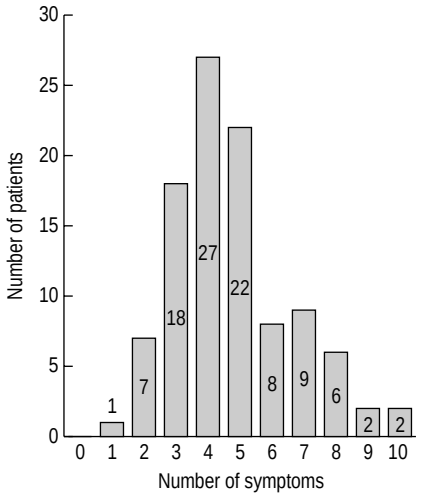


Fig. 4 Patient distribution for number of symptoms experienced of the symptoms (10) of early schizophrenia, which were observed with high frequency or more than 1/3

Treatment

Lastly, treatment of early schizophrenia is discussed briefly. The first concerns the attitude of the treating physician. In order to respond to the patient's tense and perplexed mood, the physician should be serious and grave above anything else.

The second concerns the techniques of interview. It is important to conduct a detailed question and answer session in order to describe the symptoms in an objective and linguistic manner. In ordinary type schizophrenia, questioning the details of hallucination and delusion is nearly always forbidden. But this is contrary in the case of early schizophrenia. Since the patient does not understand the experience he is undergoing and is extremely uneasy and tense, asking detailed questions will cause the patient to view these experi-

ences in an objective way and to recognize the same as something different from his original character. In other words, putting distance between him and the symptoms is effective for treatment.

Thirdly, the author usually administers 100–300 mg/day of sulpride as a drug of the first choice. This drug alone improves about 1/2 to 2/3 of the patients. If this is not effective enough, the dose may be increased to 600 mg/day, or a small amount of fluphenazine (about 0.75–1.5 mg/day) may be administered additionally. (Anti-parkinsonism agent should always be dosed concurrently in order to prevent extrapyramidal side effects.) It is, however, true that there are a considerable number of cases which utterly fail to respond to this treatment regimen.

Fourthly, it is essential to determine and tell the patient that he is suffering from a disease of the brain, for which he is not responsible. Almost all the patients are relieved to hear this. A patient related later "I wouldn't have known what to do if I was told that I was not ill". As for the name of the disease, telling the patient that he is suffering from early schizophrenia may even in this day drive him to suicide. Therefore, the author usually tells that the patient is suffering from "oversensitive disorder", a name that may be false. However, this naming seems to be adequate to describe the experiences or symptoms of the patient and appears to be acceptable. At any rate, the important thing is the physician's recognition that the patient is suffering from a disease, irrespective of the name.

Conclusion

The clinical picture of "early schizophrenia", a clinical entity proposed by the author, was discussed. The author would like to conclude that only a limited number of patients can positively describe the details of their abnormal experiences (they appear to be truly inexplicable), and therefore many of such patients are misdiagnosed as "school refusal", "adolescence crisis", "depressive state", or "too nervous". The author hopes that this paper would be of some use for daily clinical scene.

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Long-term Follow-up of an Elderly Patient with Ankylosis of the Temporomandibular Joint: Case Report

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Abstract: An 84-year-old woman with ankylosis of the temporomandibular joint underwent bilateral arthroplasty and was followed up for 10 years. At age 81 and 82, she underwent arthroplasty at another hospital but severe osseous ankylosis remained. Bilateral ramiresection and reconstruction of the temporomandibular joint were conducted using silastic sheet with dacron mesh as the interposition. The degree of mouth opening increased from 0 to 34 mm. The patient exercised jaw movement with a mouth opener and mouth opening was retained at 27–30 mm.

Key words: Ankylosis; Temporomandibular joint; Elderly patient; Long-term follow-up

Introduction

With the aging of Japan's population, masticatory function in the elderly has become a problem. Long-term follow-up of patients with ankylosis of the temporomandibular joint are needed after temporomandibular treatment. Either conservative treatment or arthroplasty is generally conducted to treat ankylosis of the temporomandibular joint. Some long-term follow-up has been reported,[1)] but that in the elderly with temporomandibular ankylosis is rare. We treated ankylosis of the temporomandibular joint in an 84-year-old woman. After surgery, we have followed her up for 10 years.

Methods

We reviewed the patient's medical charts and interviewed her and her family about the outcome of treatment.

Case Report

An 84-year-old woman consulted us in 1989 due to trismus causing difficulty in eating. In 1983 or 1984, bilateral temporomandibular disorder appeared. The cause of this condition was unknown. The rheumatoid factor was negative. In 1986 and 1987, arthroplasty of the temporomandibular joint was conducted at another hospital and articular discs were removed. After these operations, osseous ankylosis occurred.

Fig. 1 Preoperative profile of the patient with temporomandibular ankylosis after exercising mouth opening. Marked trismus is still evident.

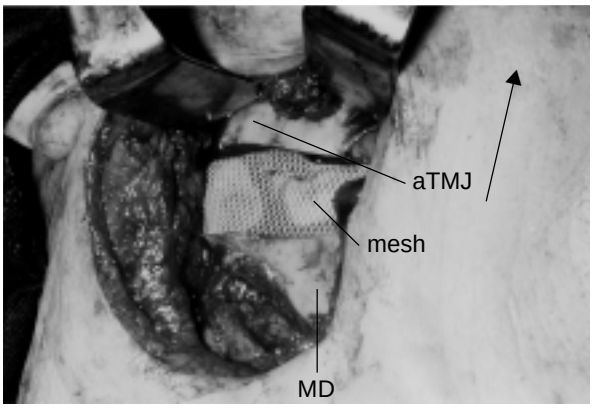

Fig. 2 Surgical view of arthroplasty.
aTMJ: ankylosed temporomandibular joint
MD: mandibular bone
←: direction of the head

Fig. 3 Postoperative profile.

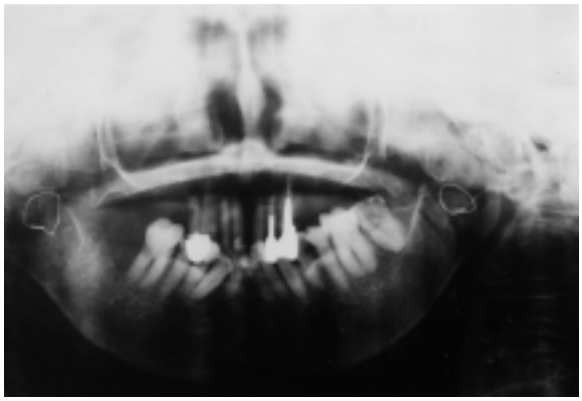

Fig. 4 Panoramic radiograph 9 years after operation.

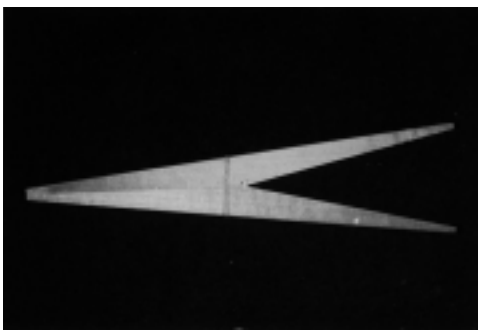

Fig. 5 Mouth opener.

Fig. 6 Postoperative profile after long-term follow-up. Mouth opening is 30 mm.

Mouth opening was 0 mm at the first medical examination and only 3 mm after mouth-opening exercises (Fig. 1). Conservative treatment with a mouth opener was not effective. Arthroplasty by open reduction was conducted in 1989, since the preoperative general condition was evaluated as fair. Incisions were made in bilateral ascending rami. Upper parts of ascending rami were cut down horizontally using a microair saw and silastic sheet with dacron mesh laid to cover the resected bones and fixed by 0.3 mm-diameter stainless steel wire[2] (Fig. 2). Bilateral pseudotemporomandibular joints were then reconstructed and incisions were closed with nylon sutures. The degree of mouth opening was 34 mm postoperatively (Fig. 3) and satisfactory mastication was achieved.

About 10 years have passed since arthroplasty (Fig. 4), during which time, the patient exercised jaw movement with a mouth opener (Fig. 5). Monthly follow-up showed no problem with pain, eating, or conversation. Mouth opening remains at 27–30 mm (Fig. 6).

Discussion

Ankylosis is commonly associated with trauma, infection, or systemic disease including rheumatoid arthritis.[3] In this case, removal of articular discs in previous operations may have caused osseous ankylosis leading to hypomorbility.

Many techniques for treating ankylosis have been described,[1–4] but successful results have not been gained by a single method. Resection of the bilateral rami followed by reconstruction of the temporomandibular joint using silastic sheet with dacron mesh as the interposition between resected bones may be classic. Given the woman's age, 84, it was dangerous to aggressively resect the ankylotic segment and coronoidectomy would require an operation time. The woman had already undergone arthroplasty, so it was not appropriate to take an intraarticular approach as the third trial because this could damage the surrounding arteries and nerves.

The present amount of mouth opening remains at 27–30 mm. Considering the mouth opening, 0 mm, before operation, the patient was quite satisfied. No problem exists with diet, and the woman has continued opening her mouth with a mouth opener, which may prevent reankylosis.

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Frequency of Falls and Bone Fractures in the Elderly

JMAJ 44(4): 192–197, 2001

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Abstract: It has been only some 10 years since the study of falls in the elderly was initiated in Japan. The frequency, or incidence, of falls depends on age, sex, ADL (Activities of Daily Living), health condition including underlying diseases, and living environment. However, the nature of such events and their preventive strategies remain unclear. In Japan, the frequency of falls in the elderly in medical and care institutions varies from approximately 10 to 40%, however, that among the elderly living at home is approximately 10 to 20% in Japan, being lower than that in foreign countries. Many studies have reported that the frequency of falls was higher in women than in men, and that it increased sharply with advancing age. Our studies showed that the incidence of fractures was approximately 10% among elderly fallers living at home, of which the rate of femoral neck fractures was estimated to be less than 10%. It is anticipated that awareness of the significance of falls and fractures will increase among ordinary people and medical professionals.

Key words: Fall; Community; The elderly; Fractures; Epidemiology

Introduction

The research on falls among the elderly started in the United Kingdom approximately 50 years ago and spread to the U.S. and the European countries. Even today, falls are considered to be an important causative factor of bone fractures and reduced mobility and as a senile syndrome. Investigators in the U.S. and Europe have been eagerly studying preventive strategies for falls.

On the other hand, in Japan, the research on falls has only been being performed for some 10 years. Although it is not possible to identify the reason why research in this field was only recently started in Japan, it may be because geriatrics itself was not fully established, and that falls were not recognized as a frequently occurring symptom among the elderly. However, the topics on falls have been broadcasted in the "Special Course in Medicine" of Nihon Shortwave Broadcasting and

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the subject of "Falls among the Elderly" was discussed at the 25th General Assembly of Japan Medical Congress. These facts indicate that the importance of falls has now been recognized in Japan.[1,2)]

Significance of Falls

This section describes the significance of falls. Falls are classified into "XX. External causes of injuries, disease, and death; sudden accident (V01-X59)" in the 10th revision of the International Classification of Diseases (ICD-10) along with traffic accidents. Among elderly people aged 65 years or older, 21,149 died of sudden accidents in 1996: the most frequent cause of death was sudden choking on foods or phlegm (25.6%), followed by traffic accidents (23.2%) and falls (17.9%) (Fig. 1). This indicates that the frequency of death as a result of falls exceeds two-thirds of that by traffic accidents. Various actions have been taken to reduce the incidence of traffic accidents involving elderly people at a national level, however, the actual situations of falls have not been fully understood, and preventive actions have only just begun to be implemented.

Falling is one of the direct causes of femoral neck fracture, which has recently been attracting widespread attention as a cause of the so-called "bed-ridden." The relative significance of femoral neck fracture has become higher because of the reduced incidence of cerebral stroke, the major cause of the bed-ridden state, thanks to improved nutritional status and living environments, and because of the increased incidence of osteoporosis due to the increase in people in the old-old elderly group of 75 years or older.

Although investigators have come to pay close attention to osteoporosis as an underlying cause of femoral neck fracture, the magnitude in which osteoporosis contributes to such fractures is not well understood. Approximately 90% of femoral neck fracture are caused by falls, including stumbling and slipping. Accordingly, investigating how elderly people fall and taking preventive strategies is the most effective way of preventing femoral neck fracture and eventually the bed-ridden state.

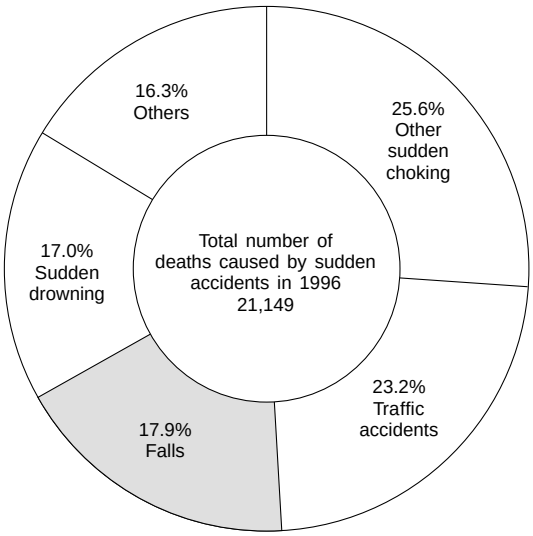

Fig. 1 Death rate due to sudden accidents in the elderly (prepared by the author according to the 1996 Vital Statistics of Population by the Ministry of Health and Welfare)

Definition of Falls

We have investigated the frequency and cause of falls as well as the current condition of fractures among elderly people in Japan. We report the results of the investigation and discuss the fractures associated with falls.

It is important to clarify the definition of falls as well as the methods of investigation and calculation when investigating the frequency of falls because it is not possible to compare studies using different definitions or methods of investigation and calculation. According to the definition of Gibson[3)] reported in 1990, we defined falls as "falling down to the ground, or to the lower level against one's will."

There are two main methods for investigating falls. One is fall registration systems based on fall records and accident reports in hospi-

Table 1 Incidence of Falls among Elderly People in Institutions

Investigator	Year	Institution and place	Number of subjects (age)	Incidence of falls (%)		
				Men	Women	Total
Rodstein	1964	Home and hospital for the elderly; New York, USA	376 (—)			25.3[a]
Gryfe Cl *et al.*	1977	Home for the elderly; Tronto, Canada	441 (65 years or older)	42.8[b]	46.2[b]	44.9[b]
Haga *et al.*	1986	Home for the elderly; Tokyo	1,406 (65 years or older)	12.0	16.2	14.5
Tokuda *et al.*	1988	Home for the elderly; Tokyo	103 (mean: 76.3 years)	9.4	21.5	12.9
Robbins AS *et al.*	1989	Home for the elderly; Los Angeles, USA	704 (mean: 88 years)			53
Gross YT *et al.*	1990	Nursing home; Honolulu, USA	178 (mean: 81.9 years)			16.3
Suzuki *et al.*	1992	Home for the elderly; Hamamatsu, Shizuoka pref.	181 (mean: 76.4 years)	30.6[c]	36.6[c]	35.4[c]
Niino and Nakamura	1996	Nursing home for the elderly; Tokyo	174 (mean: 78.2 years)	31	39	37

Incidence of falls = (number of people who fell during the investigation period / subjects) × 100
Investigation period: [a] = months, [b] = 5 years, [c] = 2 years, no mark = 1 year (including the values converted to 1 year)

tals or nursing homes for the elderly. The staff of such institutions records every fall occurring among the patients (elderly people) in their institutions. The other method is by interviews with the elderly on falls experienced during the last 1 year. This latter method is also used for those elderly people living at home by sending questionnaires to their homes and asking very simple questions, such as "Have you fallen in the last 1 year?" to obtain yes / no answers. Because this method is dependent upon the memories of the elderly subjects, it has several disadvantages, such as the tendency to underestimate the frequency and the lack of accurate data for those with dementia. However, it has been shown to provide generally reliable data with their memories back to 1 year, it is thus mainly used in the areas where frequent investigations cannot be performed.[4)]

The frequency of fracture has been investigated not only using the method based on the memory of subjects, but also via the use of health insurance records of reimbursement (Recepts) because it is anticipated that the majority of those patients who sustain fractures will visit medical institutions. Since almost all the patients with femoral neck fracture are expected to visit medical institutions, it is possible to investigate the incidence of such fractures by sending out a questionnaire to all the medical institutions with departments of orthopedics, surgery, and rehabilitation within the region.

Frequency of Falls and Fracture: Differences among Institutions, Hospitals, and Communities

The frequency or incidence of falls depends on age, sex, activities of daily living (ADL), health condition including diseases, and living environments.

The frequency of falls among elderly patients living in institutions varies from about 10 to 50% (Table 1).[5)] Such a large difference in the frequency may be a result of differences in the type of institutions, for example, between nursing homes for the elderly that are equipped with sufficient measures to prevent falls, such as hand rails and anti-skid floors, and general homes for the elderly that

Table 2 Incidence of Falls among Elderly People Living at Home in Japan

Investigator	Year	Area	Number of subjects (age)		Incidence of falls (%)		
			Men	Women	Men	Test	Women
Yasumura *et al.*	1991	Nangai village, Akita pref.	276 (71.8±5.8)	409 (72.4±6.1)	19.2	ns	20.3
Yasumura *et al.*	1994	Koganei, Tokyo	366 (71.6)	441 (72.1)	12.8	$p<0.01$	21.5
Yasumura *et al.*	1996	Nakasato village, Niigata pref.	532 (73.1)	785 (74.4)	17.7	ns	20.6
Kano *et al.*	1997	Hamamatsu, Shizuoka pref.	219 (65 years or older)	315 (65 years or older)	18.7	ns	22.9
Sakihara *et al.*	1997	Urasoe, Okinawa pref.	340 (Mean for men and women: 74.0 years)	497	6.8	$p<0.05$	13.7
Haga	1997	Otofuke, Hokkaido	369 (72.0)	481 (72.4)	16.4	ns	19.1
Niino	1997	Koganei, Tokyo	285 (75.8±5.1)	339 (76.2±5.1)	9.5	$p<0.05$	14.8

lack such preventive measures. It is also possible that there may be substantial differences among institutions in the health conditions of elderly people who are resident there, which may in turn, result in a difference in the frequency of falls.

Medical institutions, such as those for rehabilitation, have reported that the frequency of falls among inpatients ranged from about 30 to 40%, although some were reported to be approximately 10%. It is necessary to interpret the data from medical institutions carefully because all the data are based on inpatients and the investigational period was not always 1 year, however, the data may be indicative of a serious situation wherein approximately one third of inpatients hospitalized for treatment and recuperation sustain injuries, occasionally resulting in death, which are caused by accident of falls.

For the frequency of falls among elderly people living at home, many previous studies in the U.S. and Europe have reported that it ranged from approximately 30 to 40%. Previous Japanese studies have reported that it ranged from less than 10% to some 20%, being lower than that of other countries (Table 2). The life expectancy of Japanese people is the longest in the world. In Tokyo and Okinawa pref. in particular, which have the greatest longevity in Japan, tend to have a slightly lower frequency of falls than other areas. Therefore, falls can be regarded as being an index of the degree of physical health. It can also be said that the long life expectancy of the Japanese may result from the fact that the country is composed of healthy people who are unlikely to fall.

It is a well-known fact that the incidence of femoral neck fracture is higher among Caucasians in the U.S. and Europe than in Japan. However, it is also reported that bone density is higher, in other words, North Americans and Europeans have harder bones. The reason why the incidence of femoral neck fracture is higher among Caucasians in the U.S. and Europe in whom the bone is considered to be hard and unlikely to be fractured relates to the frequency of falls. Elderly people in Japan do not suffer from femoral neck fracture

because of the lower frequency of falls.[6)]

Our investigation has shown that the incidence of fractures caused by falls among elderly people living at home is approximately 10% (8.7% in men and 11.5% in women). The rate of femoral neck fracture among all types of fractures is considered to be less than 10%. Assuming that approximately 20% of elderly people living at home fall once a year, it is expected that fractures occur in approximately 2%, and femoral neck fractures in about 0.2%, annually.

Frequency of Falls and Fracture: Difference in Sex

For the difference in sex in the frequency of falls and fractures, our investigation in rural areas, such as Nangai village in Akita pref. and Nakasato village in Niigata pref., has demonstrated the frequency to be higher in women (approximately 20%) than in men (17 to 19%) (Table 2). An examination of the standing position holding function of the subjects with a gravity center oscillation meter showed that the center of gravity was more oscillated in women than in men in all the age groups examined. Many studies have agreed on the higher frequency of falls in women than in men, and this may be partially explained by the difference in the above balance function.

Frequency of Falls and Fracture: Difference in Age

Many studies have reported the frequency of falls in the old-old elderly group (75 years or older) to be significantly higher than that in the young-old elderly group (74 years or younger), suggesting that the frequency sharply increased with advancing age. This tendency was seen in all the areas and subject groups examined. A national survey on the incidence of femoral neck fracture conducted in 1992 has shown that approximately 77,000 new cases with the fracture were found within the year, and that the incidence in women was approximately 0.1% in their sixties, 0.4% in their seventies, 1.4% in their eighties, and 2.6% in their nineties, indicating the sharp increase with advancing age.[7)] The sharp increase in femoral neck fracture in the old-old elderly group in spite of an annual reduction of bone density of only about 1 to 2% suggests that falls largely contribute to femoral neck fracture, when compared to osteoporosis.

It is clear, considering the projected future increases in the numbers of people in the old-old elderly group, that this factor may adversely contribute to an increase in the frequency of falls and thus to the incidence of femoral neck fracture.

Factors Influencing the Frequency of Falls and Fractures and Preventive Measures

The frequency of falls and fractures is closely related to the factors and causes of falls, as described in the above.

Some institutions have started local activities to prevent falls. For example, the Hamamatsu Municipal Public Health Center in Shizuoka Prefecture has been providing a lecture meeting system entitled "Look before you leap."[8)] This is intended to investigate and prevent falls among the elderly as part of health education. They have also published and distributed free brochures, "Look before you leap," which contain the results of their investigations. This has increased the awareness of falls among the elderly and has contributed to making them realize that falls should and can be prevented. Such preventive activities in Japan are far behind those being conducted in the U.S. and Europe, however, they are gradually becoming more widespread.

Conclusion

This paper outlines the frequency of falls and fractures in the elderly. Numerous issues concerning falls and fractures including their frequency remain to be examined. It is anticipated that more investigators will become aware of the significance of such studies.

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